

=> b reg  
FILE 'REGISTRY' ENTERED AT 11:58:55 ON 16 NOV 2005  
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STRUCTURE FILE UPDATES: 15 NOV 2005 HIGHEST RN 868125-94-4  
DICTIONARY FILE UPDATES: 15 NOV 2005 HIGHEST RN 868125-94-4

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TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

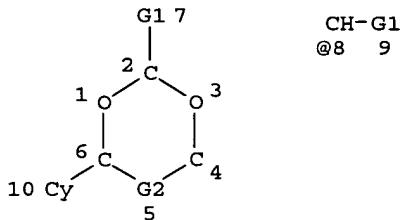
\*\*\*\*\*  
\*  
\* The CA roles and document type information have been removed from \*  
\* the IDE default display format and the ED field has been added, \*  
\* effective March 20, 2005. A new display format, IDERL, is now \*  
\* available and contains the CA role and document type information. \*  
\*  
\*\*\*\*\*

Structure search iteration limits have been increased. See HELP SLIMITS  
for details.

REGISTRY includes numerically searchable data for experimental and  
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experimental property data in the original document. For information  
on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

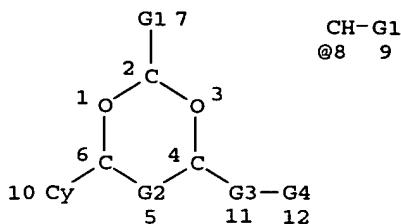
=> d que sta 130  
L16 STR



VAR G1=AK/CY  
VAR G2=CH2/8  
NODE ATTRIBUTES:  
CONNECT IS M3 RC AT 4  
DEFAULT MLEVEL IS ATOM  
GGCAT IS UNS AT 10  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 10

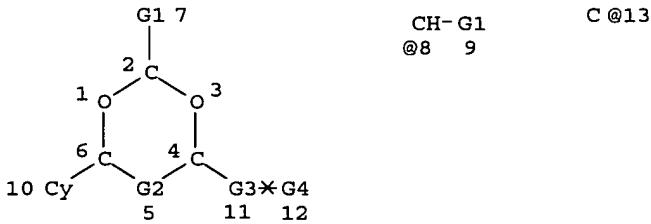
STEREO ATTRIBUTES: NONE  
L18 567 SEA FILE=REGISTRY SSS FUL L16  
L19 STR



VAR G1=AK/CY  
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 REP G3=(1-5) C  
 VAR G4=O/S  
 NODE ATTRIBUTES:  
 CONNECT IS M3 RC AT 4  
 DEFAULT MLEVEL IS ATOM  
 GGCAT IS UNS AT 10  
 DEFAULT ECLEVEL IS LIMITED

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STEREO ATTRIBUTES: NONE  
 L21 82 SEA FILE=REGISTRY SUB=L18 SSS FUL L19  
 L26 STR



VAR G1=AK/CY  
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 REP G3=(1-3) 13  
 VAR G4=N/C  
 NODE ATTRIBUTES:  
 NSPEC IS RC AT 13  
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 GGCAT IS UNS AT 10  
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
 RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 13

STEREO ATTRIBUTES: NONE  
 L27 9 SEA FILE=REGISTRY SUB=L18 SSS SAM L26  
 L28 88 SEA FILE=REGISTRY ABB=ON PLU=ON (L21 OR L27)  
 L30 79 SEA FILE=REGISTRY ABB=ON PLU=ON L28 NOT CCS/CI

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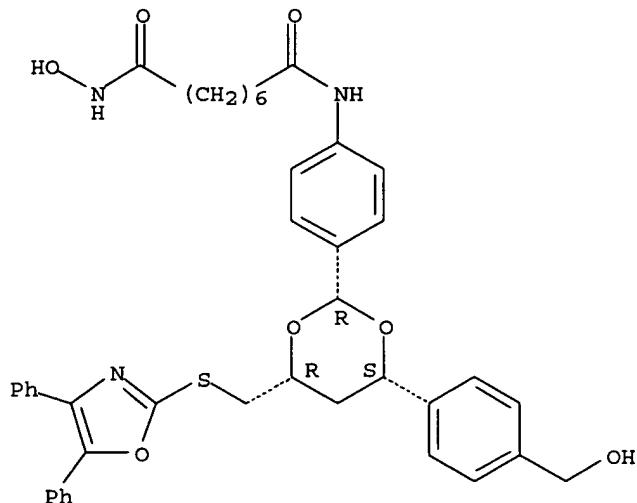
L23 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN  
 RN 537049-40-4 REGISTRY  
 ED Entered STN: 25 Jun 2003  
 CN Octanediamide, N-[4-[(2R,4R,6S)-4-[[{(4,5-diphenyl-2-oxazolyl)thio]methyl}-

6-[4-(hydroxymethyl)phenyl]-1,3-dioxan-2-yl]phenyl]-N'-hydroxy-, rel-  
(9CI) (CA INDEX NAME)

## OTHER NAMES:

CN Tubacin  
FS STEREOSEARCH  
MF C41 H43 N3 O7 S  
SR CA  
LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER, USPATFULL

Relative stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

8 REFERENCES IN FILE CA (1907 TO DATE)  
8 REFERENCES IN FILE CAPLUS (1907 TO DATE)

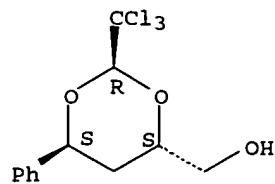
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REFERENCE 3: 142:475590  
REFERENCE 4: 142:235358  
REFERENCE 5: 140:339332  
REFERENCE 6: 140:124434  
REFERENCE 7: 139:94978  
REFERENCE 8: 139:17111

=> d ide can 145 tot

L45 ANSWER 1 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN  
RN 385372-89-4 REGISTRY  
ED Entered STN: 22 Jan 2002  
CN 1,3-Dioxane-4-methanol, 6-phenyl-2-(trichloromethyl)-, (2R,4S,6S)-rel-  
(9CI) (CA INDEX NAME)  
FS STEREOSEARCH

MF C12 H13 Cl3 O3  
 SR CA  
 LC STN Files: CA, CAPLUS

Relative stereochemistry.



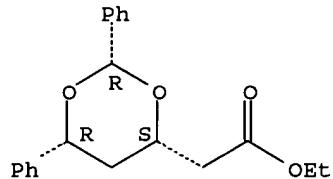
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1 REFERENCES IN FILE CA (1907 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:69857

L45 ANSWER 2 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN  
 RN 337508-83-5 REGISTRY  
 ED Entered STN: 23 May 2001  
 CN 1,3-Dioxane-4-acetic acid, 2,6-diphenyl-, ethyl ester, (2R,4S,6R)- (9CI)  
 (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C20 H22 O4  
 SR CA  
 LC STN Files: CA, CAPLUS, CASREACT

Absolute stereochemistry. Rotation (+).



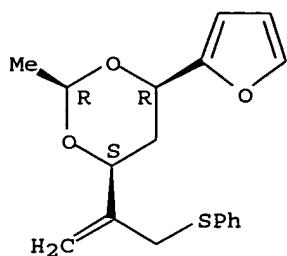
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1 REFERENCES IN FILE CA (1907 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:340467

L45 ANSWER 3 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN  
 RN 159558-15-3 REGISTRY  
 ED Entered STN: 14 Dec 1994  
 CN 1,3-Dioxane, 4-(2-furanyl)-2-methyl-6-[1-[(phenylthio)methyl]ethenyl]-, (2 $\alpha$ ,4 $\alpha$ ,6 $\alpha$ )- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C18 H20 O3 S  
 SR CA  
 LC STN Files: CA, CAPLUS, CASREACT

Relative stereochemistry.



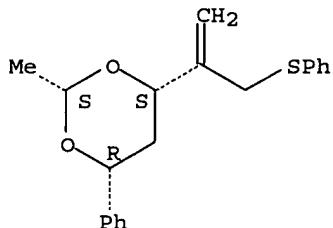
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1 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 122:30928

L45 ANSWER 4 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN  
 RN 159558-14-2 REGISTRY  
 ED Entered STN: 14 Dec 1994  
 CN 1,3-Dioxane, 2-methyl-4-phenyl-6-[(1-[(phenylthio)methyl]ethenyl)-, (2α,4α,6α)- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C20 H22 O2 S  
 SR CA  
 LC STN Files: CA, CAPLUS, CASREACT

Relative stereochemistry.



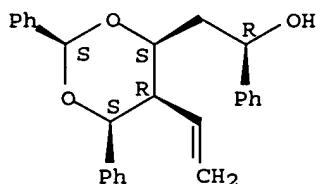
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 122:30928

L45 ANSWER 5 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN  
 RN 131349-73-0 REGISTRY  
 ED Entered STN: 11 Jan 1991  
 CN 1,3-Dioxane-4-ethanol, 5-ethenyl-α,2,6-triphenyl-, [2α,4α(S\*) ,5α,6α]- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C26 H26 O3  
 SR CA  
 LC STN Files: BEILSTEIN\*, CA, CAPLUS  
 (\*File contains numerically searchable property data)

Relative stereochemistry.



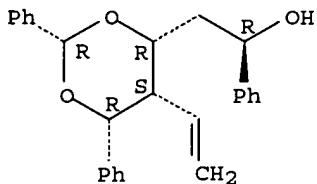
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1 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 114:207415

L45 ANSWER 6 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN  
RN 131139-31-6 REGISTRY  
ED Entered STN: 21 Dec 1990  
CN 1,3-Dioxane-4-ethanol, 5-ethenyl- $\alpha$ ,2,6-triphenyl-,  
[2 $\alpha$ ,4 $\alpha$ (R\*),5 $\alpha$ ,6 $\alpha$ ]- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C26 H26 O3  
SR CA  
LC STN Files: BEILSTEIN\*, CA, CAPLUS, CASREACT  
(\*File contains numerically searchable property data)

Relative stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

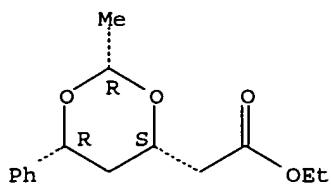
2 REFERENCES IN FILE CA (1907 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 114:185675

REFERENCE 2: 114:24103

L45 ANSWER 7 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN  
RN 130822-20-7 REGISTRY  
ED Entered STN: 07 Dec 1990  
CN 1,3-Dioxane-4-acetic acid, 2-methyl-6-phenyl-, ethyl ester,  
(2 $\alpha$ ,4 $\alpha$ ,6 $\alpha$ )- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN 1,3-Dioxane-4-acetic acid, 2-methyl-6-phenyl-, ethyl ester,  
(2 $\alpha$ ,4 $\alpha$ ,6 $\alpha$ )-( $\pm$ )-  
FS STEREOSEARCH  
MF C15 H20 O4  
SR CA  
LC STN Files: BEILSTEIN\*, CA, CAPLUS  
(\*File contains numerically searchable property data)

Relative stereochemistry.



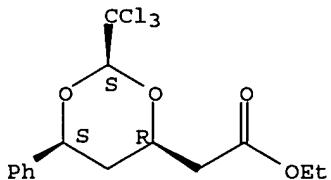
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1 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 114:6220

L45 ANSWER 8 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN  
RN 128316-91-6 REGISTRY  
ED Entered STN: 20 Jul 1990  
CN 1,3-Dioxane-4-acetic acid, 6-phenyl-2-(trichloromethyl)-, ethyl ester,  
(2 $\alpha$ ,4 $\alpha$ ,6 $\alpha$ )- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
DR 130979-26-9  
MF C15 H17 Cl3 O4  
SR CA  
LC STN Files: BEILSTEIN\*, CA, CAPLUS  
(\*File contains numerically searchable property data)

Relative stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

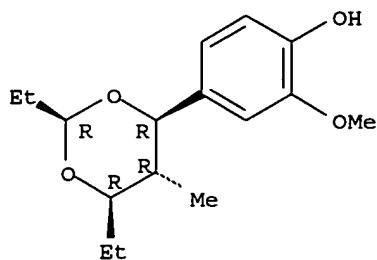
2 REFERENCES IN FILE CA (1907 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 114:6220

REFERENCE 2: 113:59054

L45 ANSWER 9 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN  
RN 104789-94-8 REGISTRY  
ED Entered STN: 18 Oct 1986  
CN Phenol, 4-(2,6-diethyl-5-methyl-1,3-dioxan-4-yl)-2-methoxy-,  
(2 $\alpha$ ,4 $\alpha$ ,5 $\beta$ ,6 $\alpha$ )- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C16 H24 O4  
SR CA  
LC STN Files: BEILSTEIN\*, CA, CAPLUS, CASREACT  
(\*File contains numerically searchable property data)

Relative stereochemistry.

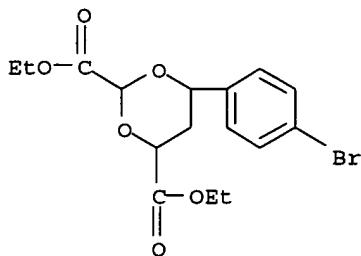


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 105:191018

L45 ANSWER 10 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN  
RN 13984-81-1 REGISTRY  
ED Entered STN: 16 Nov 1984  
CN m-Dioxane-2,4-dicarboxylic acid, 6-(p-bromophenyl)-, diethyl ester (8CI)  
(CA INDEX NAME)  
FS 3D CONCORD  
MF C16 H19 Br O6  
LC STN Files: CA, CAPLUS

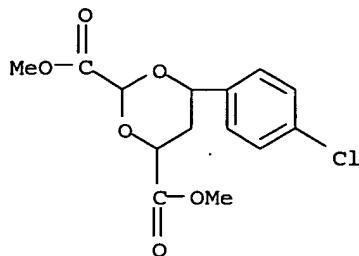


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 66:115660

L45 ANSWER 11 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN  
RN 13984-80-0 REGISTRY  
ED Entered STN: 16 Nov 1984  
CN m-Dioxane-2,4-dicarboxylic acid, 6-(p-chlorophenyl)-, dimethyl ester (8CI)  
(CA INDEX NAME)  
FS 3D CONCORD  
MF C14 H15 Cl O6  
LC STN Files: CA, CAPLUS



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1907 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 66:115660

=> b hcap  
 FILE 'HCAPLUS' ENTERED AT 11:59:44 ON 16 NOV 2005  
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FILE COVERS 1907 - 16 Nov 2005 VOL 143 ISS 21  
 FILE LAST UPDATED: 15 Nov 2005 (20051115/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all  
 YOU HAVE REQUESTED DATA FROM FILE 'USPATFULL' - CONTINUE? (Y)/N:n

=> d all 138 fhitstr tot

L38 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2005:554344 HCAPLUS  
 DN 143:109212  
 ED Entered STN: 27 Jun 2005  
 TI Small-molecule inhibition of proteasome and aggresome function induces synergistic antitumor activity in multiple myeloma  
 AU Hideshima, Teru; Bradner, James E.; Wong, Jason; Chauhan, Dharminder;  
 Richardson, Paul; Schreiber, Stuart L.; Anderson, Kenneth C.  
 CS Jerome Lipper Multiple Myeloma Center, Department of Medical Oncology,  
 Dana-Farber Cancer Institute, Harvard Medical School, Boston,  
 MA, 02115, USA  
 SO Proceedings of the National Academy of Sciences of the United States of America (2005), 102(24), 8567-8572

CODEN: PNASA6; ISSN: 0027-8424

PB National Academy of Sciences

DT Journal

LA English

CC 1-6 (Pharmacology)

AB The authors have shown that the proteasome inhibitor bortezomib (formerly known as PS-341) triggers significant antitumor activity in multiple myeloma (MM) in both preclin. models and patients with relapsed refractory disease. Recent studies have shown that unfolded and misfolded ubiquitininated proteins are degraded not only by proteasomes, but also by aggresomes, dependent on histone deacetylase 6 (HDAC6) activity. The authors therefore hypothesized that inhibition of both mechanisms of protein catabolism could induce accumulation of ubiquitininated proteins followed by significant cell stress and cytotoxicity in MM cells. To prove this hypothesis, the authors used bortezomib and tubacin to inhibit the proteasome and HDAC6, resp. Tubacin specifically triggers acetylation of  $\alpha$ -tubulin as a result of HDAC6 inhibition in a dose- and time-dependent fashion. It induces cytotoxicity in MM cells at 72 h with an IC<sub>50</sub> of 5-20  $\mu$ M, which is mediated by caspase-dependent apoptosis; no toxicity is observed in normal peripheral blood mononuclear cells. Tubacin inhibits the interaction of HDAC6 with dynein and induces marked accumulation of ubiquitininated proteins. It synergistically augments bortezomib-induced cytotoxicity by c-Jun N-terminal kinase/caspase activation. Importantly, this combination also induces significant cytotoxicity in plasma cells isolated from MM patient bone marrow. Finally, adherence of MM cells to bone marrow stromal cells confers growth and resistance to conventional treatments; in contrast, the combination of tubacin and bortezomib triggers toxicity even in adherent MM cells. Our studies therefore demonstrate that tubacin combined with bortezomib mediates significant anti-MM activity, providing the framework for clin. evaluation of combined therapy to improve patient outcome in MM.

ST bortezomib tubacin antitumor multiple myeloma

IT Drug resistance

(antitumor; small-mol. inhibition of proteasome and aggresome function induces synergistic antitumor activity in multiple myeloma)

IT Antitumor agents

(resistance to; small-mol. inhibition of proteasome and aggresome function induces synergistic antitumor activity in multiple myeloma)

IT Adhesion, biological

Antitumor agents

Combination chemotherapy

Human

Multiple myeloma

(small-mol. inhibition of proteasome and aggresome function induces synergistic antitumor activity in multiple myeloma)

IT Dyneins

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(small-mol. inhibition of proteasome and aggresome function induces synergistic antitumor activity in multiple myeloma)

IT Drug interactions

(synergistic; small-mol. inhibition of proteasome and aggresome function induces synergistic antitumor activity in multiple myeloma)

IT Proteins

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(ubiquitininated; small-mol. inhibition of proteasome and aggresome function induces synergistic antitumor activity in multiple myeloma)

IT 9076-57-7, Histone deacetylase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(6; small-mol. inhibition of proteasome and aggresome function induces synergistic antitumor activity in multiple myeloma)

IT 9055-67-8, Poly(ADP-ribose) polymerase 155215-87-5, JNK kinase  
169592-56-7, Caspase-3 179241-78-2, Caspase 8 180189-96-2, Caspase 9

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(small-mol. inhibition of proteasome and aggresome function induces synergistic antitumor activity in multiple myeloma)

IT 179324-69-7, Bortezomib 537049-40-4, Tubacin

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (small-mol. inhibition of proteasome and aggresome function induces  
 synergistic antitumor activity in multiple myeloma)

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Attal, M; N Engl J Med 2003, V349, P2495 HCAPLUS
- (2) Bennett, E; Mol Cell 2005, V17, P351 HCAPLUS
- (3) Catley, L; Blood 2003, V102, P2615 HCAPLUS
- (4) Chauhan, D; Cancer Res 2003, V63, P6174 HCAPLUS
- (5) Garcia-Mata, R; Traffic 2002, V3, P388 HCAPLUS
- (6) Gregory, W; J Clin Oncol 1992, V10, P334 MEDLINE
- (7) Haggarty, S; Chem Biol 2003, V10, P383 HCAPLUS
- (8) Haggarty, S; Proc Natl Acad Sci USA 2003, V100, P4389 HCAPLUS
- (9) Hideshima, T; Blood 2003, V101, P1530 HCAPLUS
- (10) Hideshima, T; Cancer Res 2001, V61, P3071 HCAPLUS
- (11) Hideshima, T; Cancer Res 2003, V63, P8428 HCAPLUS
- (12) Hideshima, T; Immunol Rev 2003, V194, P164 HCAPLUS
- (13) Hideshima, T; J Biol Chem 2002, V277, P16639 HCAPLUS
- (14) Hideshima, T; Nat Rev Cancer 2002, V2, P927 HCAPLUS
- (15) Hideshima, T; Oncogene 2001, V20, P4519 HCAPLUS
- (16) Hideshima, T; Oncogene 2003, V22, P8386 HCAPLUS
- (17) Hideshima, T; Oncogene 2004, V23, P8766 HCAPLUS
- (18) Kawaguchi, Y; Cell 2003, V115, P727 HCAPLUS
- (19) Kopito, R; Trends Cell Biol 2000, V10, P524 HCAPLUS
- (20) Le Gouill, S; Blood 2004, V104, P2886 HCAPLUS
- (21) Marks, P; Curr Opin Pharmacol 2003, V3, P344 HCAPLUS
- (22) Mitsiades, C; Cancer Cell 2004, V5, P221 HCAPLUS
- (23) Mitsiades, N; Blood 2003, V101, P2377 HCAPLUS
- (24) Mitsiades, N; Blood 2003, V101, P4055 HCAPLUS
- (25) Mitsiades, N; Proc Natl Acad Sci USA 2002, V99, P14374 HCAPLUS
- (26) Raje, N; Blood 2004, V104, P4188 HCAPLUS
- (27) Richardson, P; N Engl J Med 2003, V348, P2609 HCAPLUS
- (28) Uchiyama, H; Blood 1993, V82, P3712 HCAPLUS
- (29) Wong, J; J Am Chem Soc 2003, V125, P5586 HCAPLUS

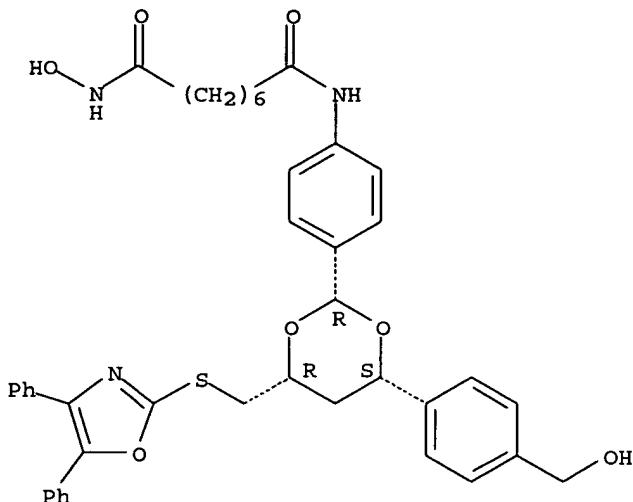
IT 537049-40-4, Tubacin

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (small-mol. inhibition of proteasome and aggresome function induces  
 synergistic antitumor activity in multiple myeloma)

RN 537049-40-4 HCAPLUS

CN Octanediamide, N-[4-[(2R,4R,6S)-4-[[[(4,5-diphenyl-2-oxazolyl)thio]methyl]-6-[(4-(hydroxymethyl)phenyl]-1,3-dioxan-2-yl]phenyl]-N'-hydroxy-, rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.



L38 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2005:497346 HCAPLUS  
 DN 143:19947  
 ED Entered STN: 10 Jun 2005  
 TI Human papillomavirus inhibitors and screening system reagentss  
 IN Meneses, Patricio I.; Koehler, Angela N.; Wong, Jason C.; Howley, Peter M.; Schreiber, Stuart L.  
 PA President and Fellows of Harvard College, USA  
 SO U.S. Pat. Appl. Publ., 23 pp.  
 CODEN: USXXCO  
 DT Patent  
 LA English  
 IC ICM C12Q001-70  
 ICS A61K031-41; C07K007-08  
 INCL 435005000; 530326000; 514381000  
 CC 1-5 (Pharmacology)  
 Section cross-reference(s): 10, 28, 63

## FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI US 2005123902	A1	20050609	US 2004-851407	20040521
PRAI US 2003-472261P	P	20030521		

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
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US 2005123902	ICM C12Q001-70 ICS A61K031-41; C07K007-08 INCL 435005000; 530326000; 514381000	
US 2005123902	NCL 435/005.000 ECLA A61K031/41	

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The present invention provides systems for identifying anti-viral agents. In particular, the invention encompasses reagents and strategies for identifying agents that inhibit or disrupt key protein-protein interactions that are important in the life cycle of papillomaviruses. The invention allows identification, production, and/or use of agents that

reduce or inhibit the replication of HPV by inhibiting (e.g., precluding, reversing, or disrupting) the formation of the E1-E2 protein-protein complex. The invention also provides specific inhibitory agents, pharmaceutical compns., and methods of using these inhibitors and pharmaceutical compns. for inhibiting viral replication in vitro. Methods are also described for the treatment and prevention of HPV infections and HPV-related diseases in patients. Example 1 relates to a binding assay used to identify small mols. capable of preventing or disrupting the formation of the HPV-16 E1-E2 complex. The assay, which was carried out to screen a small mol. library of 1,3-dioxanes, led to the identification of compound 1 (I), along with nine other leads. Example 2 describes the synthesis of compds. 2 (II) and 3 (III), which are two enantiomers of a derivative of compound 1. Example 3 illustrates the determination by surface plasmon resonance of the equilibrium dissociation consts. for the binding of compound 2 and compound 3 to the HPV-16 E2 protein. Example 4 describes biol. assays that can be used to demonstrate the disruption of the E1-E2 protein-protein binding induced by compds. 2 and 3 in vitro.

- ST papillomavirus inhibitor screening E1 E2 complex disruption; HPV16 E1 E2 complex inhibitor dioxane compd; surface plasmon resonance screening HPV inhibitor
- IT Proteins
  - RL: BSU (Biological study, unclassified); BIOL (Biological study) (E1, association with E2, disruption or prevention of; human papillomavirus inhibitors and screening system reagents)
- IT Drug targets
  - (E1-E2 complex; human papillomavirus inhibitors and screening system reagents)
- IT Proteins
  - RL: BSU (Biological study, unclassified); BIOL (Biological study) (E2, association with E1, disruption or prevention of; human papillomavirus inhibitors and screening system reagents)
- IT Proteins
  - RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DEV (Device component use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
    - (E2, fusion protein with GST, complexes with anti-GST flow cells, small mol. binding to; human papillomavirus inhibitors and screening system reagents)
- IT Immobilization, molecular or cellular
  - (antibody; human papillomavirus inhibitors and screening system reagents)
- IT Fluorescent substances
  - (as labels in screening system; human papillomavirus inhibitors and screening system reagents)
- IT Disease, animal
  - (associated with viral infection, treatment of; human papillomavirus inhibitors and screening system reagents)
- IT Uterus, disease
  - (cervix, dysplasia, treatment of, as disease associated with HPV-16; human papillomavirus inhibitors and screening system reagents)
- IT Uterus, neoplasm
  - (cervix, treatment of, as disease associated with HPV-16; human papillomavirus inhibitors and screening system reagents)
- IT Antiviral agents
  - Drug delivery systems
  - Drug screening
  - Fluorometry
  - Human
    - Human papillomavirus
    - Human papillomavirus 16
    - Human papillomavirus 18
    - Human papillomavirus 31
    - Human papillomavirus 33
    - Papillomavirus
    - Prophylaxis
    - Surface plasmon resonance

(human papillomavirus inhibitors and screening system reagents)

IT Antibodies and Immunoglobulins  
 RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DEV (Device component use); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (immobilized, to GST, on CMS sensor chip; human papillomavirus inhibitors and screening system reagents)

IT Biosensors  
 (immunol., optical, surface plasmon-based; human papillomavirus inhibitors and screening system reagents)

IT Peptides, biological studies  
 RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); CUS (Combinatorial use); ANST (Analytical study); BIOL (Biological study); CMPI (Combinatorial study); USES (Uses)  
 (in screening system; human papillomavirus inhibitors and screening system reagents)

IT Virus replication  
 (inhibition of; human papillomavirus inhibitors and screening system reagents)

IT Molecular association  
 (protein-protein interaction, E1-E2; human papillomavirus inhibitors and screening system reagents)

IT Chemical library  
 (screening of; human papillomavirus inhibitors and screening system reagents)

IT Molecules  
 (small, library, screening of; human papillomavirus inhibitors and screening system reagents)

IT Infection  
 (viral, treatment and prevention of; human papillomavirus inhibitors and screening system reagents)

IT 852992-28-0  
 RL: BSU (Biological study, unclassified); CST (Combinatorial study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMPI (Combinatorial study); USES (Uses)  
 (as antiviral agent inhibiting papillomavirus replication; human papillomavirus inhibitors and screening system reagents)

IT 852992-29-1P 852992-30-4P  
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (as antiviral agent inhibiting papillomavirus replication; human papillomavirus inhibitors and screening system reagents)

IT 852992-26-8  
 RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); CUS (Combinatorial use); PRP (Properties); ANST (Analytical study); BIOL (Biological study); CMPI (Combinatorial study); USES (Uses)  
 (as interacting peptide in screening system; human papillomavirus inhibitors and screening system reagents)

IT 146368-14-1, Cy5  
 RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); CUS (Combinatorial use); ANST (Analytical study); BIOL (Biological study); CMPI (Combinatorial study); USES (Uses)  
 (as label in screening system; human papillomavirus inhibitors and screening system reagents)

IT 852992-27-9  
 RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); CUS (Combinatorial use); PRP (Properties); ANST (Analytical study); BIOL (Biological study); CMPI (Combinatorial study); USES (Uses)  
 (as specificity peptide in screening system; human papillomavirus inhibitors and screening system reagents)

IT 13183-79-4, 5-Mercapto-1-methyltetrazole 475160-79-3D, resin-bound  
 475160-80-6D, resin-bound 475160-91-9  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (human papillomavirus inhibitors and screening system reagents)

IT 852992-29-1DP, resin-bound 852992-31-5DP, resin-bound

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (human papillomavirus inhibitors and screening system reagents)

IT 50812-37-8, Glutathione S transferase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (immobilization of antibody to; human papillomavirus inhibitors and screening system reagents)

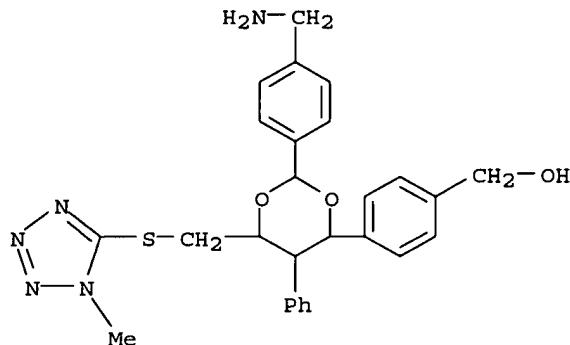
IT 505-22-6D, 1,3-Dioxane, compds.  
 RL: BSU (Biological study, unclassified); CST (Combinatorial study, unclassified); BIOL (Biological study); CMBI (Combinatorial study)  
 (screening library of; human papillomavirus inhibitors and screening system reagents)

IT 50812-37-8D, Glutathione S transferase, fusion proteins with E2 protein, complexes with anti-GST flow cells  
 RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DEV (Device component use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (small mol. binding to; human papillomavirus inhibitors and screening system reagents)

IT 852992-28-0  
 RL: BSU (Biological study, unclassified); CST (Combinatorial study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); USES (Uses)  
 (as antiviral agent inhibiting papillomavirus replication; human papillomavirus inhibitors and screening system reagents)

RN 852992-28-0 HCAPLUS

CN Benzenemethanol, 4-[2-[4-(aminomethyl)phenyl]-6-[[[(1-methyl-1H-tetrazol-5-yl)thio]methyl]-5-phenyl-1,3-dioxan-4-yl]- (9CI) (CA INDEX NAME)



L38 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2004:878826 HCAPLUS  
 DN 142:235358  
 ED Entered STN: 22 Oct 2004  
 TI Mapping chemical space using molecular descriptors and chemical genetics:  
 Deacetylase inhibitors  
 AU Haggarty, Stephen J.; Clemons, Paul A.; Wong, Jason C.; Schreiber,  
 Stuart L.  
 CS The Eli and Edythe L. Broad Institute, Massachusetts Institute of  
 Technology and Harvard University, Cambridge, MA, 02141, USA  
 SO Combinatorial Chemistry and High Throughput Screening (2004), 7(7),  
 669-676  
 CODEN: CCHSFU; ISSN: 1386-2073  
 PB Bentham Science Publishers Ltd.  
 DT Journal  
 LA English  
 CC 7-3 (Enzymes)  
 AB An objective of chemical genetics is to understand the relationships between  
 the structures of small mols. and their phenotypic effects in intact

living systems. We present here the results of a global anal. of a mol. descriptor space constructed using structural descriptors of an aryl 1,3-dioxane-based diversity-oriented synthesis-derived library containing structural biasing elements directed at inhibiting protein deacetylases. Using principal component anal. and three-dimensional visualization, we generated metric space maps with morphol. features contributed by different diversity elements within the library. Filtering these maps using phenotypic descriptors derived from measurements of small-mol. activities in an array of cell-based assays revealed different densities of biol. activity within specific subspaces. These results provide evidence that certain structural features may be important for conferring potency and selectivity on deacetylase inhibitors with respect to tubulin and histone acetylation. Moreover, these results highlight an example of the importance of using functional measures to assess mol. diversity. Similar analyses of other chemical spaces and activity classes promise to facilitate the development of chemical genetics.

- ST dioxane deriv mol descriptor protein deacetylase inhibitor  
 IT Combinatorial library  
     (aryl 1,3-dioxane-based; global anal. of mol. descriptor space  
     constructed using structural descriptors of aryl 1,3-dioxanes as  
     protein deacetylase inhibitors)  
 IT Principal component analysis  
     (global anal. of mol. descriptor space constructed using structural  
     descriptors of aryl 1,3-dioxanes as protein deacetylase inhibitors)  
 IT Histones  
 Tubulins  
     RL: BSU (Biological study, unclassified); BIOL (Biological study)  
     (global anal. of mol. descriptor space constructed using structural  
     descriptors of aryl 1,3-dioxanes as protein deacetylase inhibitors)  
 IT Structure-activity relationship  
     (protein deacetylase inhibitor; global anal. of mol. descriptor space  
     constructed using structural descriptors of aryl 1,3-dioxanes as  
     protein deacetylase inhibitors)  
 IT 9076-57-7, Histone deacetylase 438496-81-2, Tubulin deacetylase  
     RL: BSU (Biological study, unclassified); BIOL (Biological study)  
     (global anal. of mol. descriptor space constructed using structural  
     descriptors of aryl 1,3-dioxanes as protein deacetylase inhibitors)  
 IT 537049-40-4, Tubacin  
     RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
     (Biological study)  
     (global anal. of mol. descriptor space constructed using structural  
     descriptors of aryl 1,3-dioxanes as protein deacetylase inhibitors)  
 RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD  
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 (2) Albert, R; Rev Mod Phys 2002, V74, P47  
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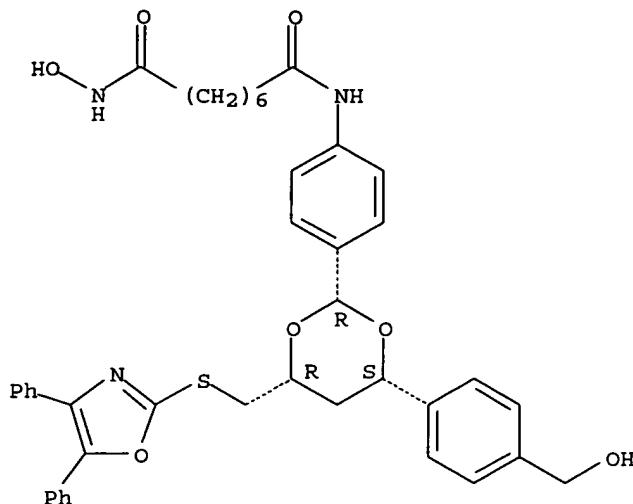
IT 537049-40-4, Tubacin

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
 (Biological study)  
 (global anal. of mol. descriptor space constructed using structural  
 descriptors of aryl 1,3-dioxanes as protein deacetylase inhibitors)

RN 537049-40-4 HCPLUS

CN Octanediamide, N-[4-[(2R,4R,6S)-4-[[[(4,5-diphenyl-2-oxazolyl)thio]methyl]-  
 6-[4-(hydroxymethyl)phenyl]-1,3-dioxan-2-yl]phenyl]-N'-hydroxy-, rel-  
 (9CI) (CA INDEX NAME)

Relative stereochemistry.



L38 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2004:775495 HCAPLUS  
 DN 142:261482  
 ED Entered STN: 23 Sep 2004  
 TI Modular synthesis and preliminary biological evaluation of stereochemically diverse 1,3-dioxanes  
 AU Wong, Jason C.; Sternson, Scott M.; Louca, Joseph B.; Hong, Roger; Schreiber, Stuart L.  
 CS Department of Chemistry and Chemical Biology, Harvard University, Cambridge, MA, 02138, USA  
 SO Chemistry & Biology (2004), 11(9), 1279-1291  
 CODEN: CBOLE2; ISSN: 1074-5521  
 PB Cell Press  
 DT Journal  
 LA English  
 CC 28-11 (Heterocyclic Compounds (More Than One Hetero Atom))  
 AB Modular synthesis and substrate stereocontrol were combined to furnish 18,000 diverse 1,3-dioxanes whose distribution in chemical space rivals that of a reference set of over 2,000 bioactive small mols. Library quality was assessed at key synthetic stages, culminating in a detailed postsynthesis anal. of purity, yield, and structural characterizability, and the resynthesis of library subsets that did not meet quality stds. The importance of this anal.-resynthesis process is highlighted by the discovery of new biol. probes through organismal and protein binding assays, and by determination of the building block and stereochem. basis for their bioactivity. This evaluation of a portion of the 1,3-dioxane library suggests that many addnl. probes for chemical genetics will be identified as the entire library becomes biol. annotated.  
 ST combinatorial library dioxane prepn atrioventricular block induction; calmodulin binding combinatorial library dioxane prepn  
 IT Heart  
     (atrionventricular node, block; modular synthesis and preliminary biol. evaluation of stereochem. diverse 1,3-dioxanes)  
 IT Calmodulins  
     RL: BSU (Biological study, unclassified); BIOL (Biological study)  
     (binding; modular synthesis and preliminary biol. evaluation of stereochem. diverse 1,3-dioxanes)  
 IT Combinatorial library  
     (modular synthesis and preliminary biol. evaluation of stereochem. diverse 1,3-dioxanes)  
 IT 505-22-6DP, 1,3-Dioxane, derivs. 845796-60-3P 845796-61-4P  
     845796-62-5P 845796-63-6P 845796-64-7P 845796-65-8P

RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation) (modular synthesis and preliminary biol. evaluation of stereochem. diverse 1,3-dioxanes)

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD  
RE

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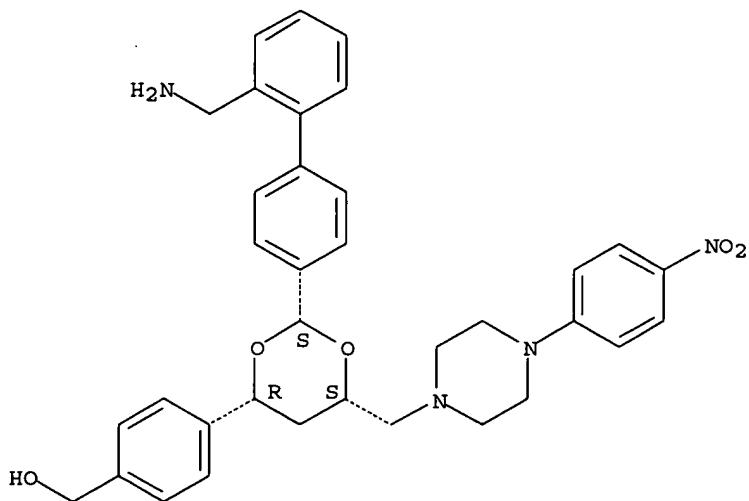
IT 845796-65-8P

RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation) (modular synthesis and preliminary biol. evaluation of stereochem. diverse 1,3-dioxanes)

RN 845796-65-8 HCPLUS

CN Benzenemethanol, 4-[(2S,4R,6S)-2-[2'-(aminomethyl)[1,1'-biphenyl]-4-yl]-6-[[4-(4-nitrophenyl)-1-piperazinyl]methyl]-1,3-dioxan-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



DN 140:339332  
 ED Entered STN: 16 Apr 2004  
 TI Preparation of trisubstituted dioxanes as histone deacetylase inhibitors.  
 IN Schreiber, Stuart L.; Sternson, Scott M.; Wong, Jason C.; Grozinger, Christina M.; Haggarty, Stephen J.; Koeller, Kathryn M.

PA USA  
 SO U.S. Pat. Appl. Publ., 177 pp., Cont.-in-part of U.S. Pat. Appl. 2003 187,027.  
 CODEN: USXXCO

DT Patent

LA English

IC ICM A61K031-52

ICS A61K031-506; A61K031-335

INCL 514263230; 514269000; 514452000; 544269000; 544310000

CC 28-11 (Heterocyclic Compounds (More Than One Hetero Atom))

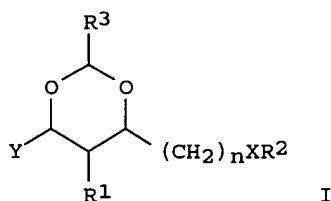
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004072849	A1	20040415	US 2003-621276	20030717 <--
	US 2003187027	A1	20031002	US 2002-144316	20020509 <--
PRAI	US 2001-289850P	P	20010509	<--	
	US 2002-144316	A2	20020509	<--	

CLASS

	PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
	US 2004072849	ICM	A61K031-52
		ICS	A61K031-506; A61K031-335
		INCL	514263230; 514269000; 514452000; 544269000; 544310000
	US 2004072849	NCL	514/263.230
		ECLA	C07D319/06; C07D405/06+319+211; C07D405/12+319+257; C07D413/12+319+263B; C07D417/12+319+277; C07D491/10+317A+221A
	US 2003187027	NCL	514/336.000
		ECLA	C07D319/06; C07D405/06+319+211; C07D405/12+319+257; C07D413/12+319+263B; C07D417/12+319+277; C07D491/10+317A+221A

OS MARPAT 140:339332  
 GI



AB Title compds. [I; R1, Y = H, aliphatic, alicyclyl, heteroaliphatic, heterocyclic, aryl, heteroaryl; n = 1-5; R2 = R1, protecting group; X = O, S, C(R2a)2, NR2a; R2R2a = atoms to form alicyclyl, heterocyclic, aryl, heteroaryl; R3 = aliphatic, alicyclic, heteroaliphatic, heterocyclic, aryl, heteroaryl], were claimed. Thus, rel-N-[4-[(2R,4R,6S)-4-[[[(4,5-diphenyl-2-oxazolyl)thiomethyl]-6-[4-(hydroxymethyl)phenyl]-1,3-dioxan-2-yl]phenyl]-N'-hydroxy-octanediamide (tubacin, claimed compound) at ≥125 nM in A549 cells strongly increased α-tubulin acetylation levels. The present invention addnl. provides methods for modulating the glucose-sensitive subset of genes downstream of Ure2p.

ST dioxane trisubstituted prep histone deacetylase inhibitor; cancer treatment aryldioxane prep

IT Solid phase synthesis  
 (combinatorial; preparation of trisubstituted dioxanes as histone

deacetylase inhibitors)

IT Antitumor agents  
Human  
(preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

IT Hydroxamic acids  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

IT Combinatorial chemistry  
(solid-phase; preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

IT Neoplasm  
(treatment; preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

IT Tubulins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
( $\alpha$ -, deacetylation inhibitors; preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

IT 537049-40-4P, Tubacin 537049-41-5P, Histacin  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(claimed compound; preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

IT 9076-57-7, Histone deacetylase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors, HDAC1 or HDAC6; preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

IT 438496-81-2, Tubulin deacetylase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

IT 475161-08-1P  
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

IT 332925-19-6P 332925-20-9P 332925-21-0P 394657-68-2P  
394657-69-3P 475161-04-7P 475161-05-8P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

IT 475160-81-7P  
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
(preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

IT 475161-07-0P  
RL: PUR (Purification or recovery); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

IT 56-91-7, 4-Aminomethylbenzoic acid 149-73-5, Trimethyl orthoformate  
505-48-6, Suberic acid 589-29-7, 1,4-Benzenedimethanol 619-66-9,  
4-Formylbenzoic acid 623-04-1, 4-Aminobenzyl alcohol 873-75-6,  
4-Bromobenzyl alcohol 1877-77-6, 3-Aminobenzyl alcohol 2227-29-4,  
Chlorodiisopropylsilane 20445-31-2 38002-45-8, 3-  
Trimethylsilylpropargyl bromide 39959-54-1, 3-Bromobenzylamine  
hydrochloride  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

IT 146952-73-0P, (4-((tert-Butyldiphenylsiloxy)methyl)phenyl)methanol  
164470-64-8P 196880-47-4P, 4-((tert-Butyldiphenylsiloxy)methyl)benzaldehyde 206537-33-9P 206537-34-0P 332925-17-4P 475160-70-4P,  
(4-(Diisopropylsilyl)phenyl)methanol 475160-73-7P 475160-74-8P  
475160-75-9P 475160-76-0P 475160-77-1P 475160-78-2P 475160-79-3P  
475160-80-6P 475160-82-8P 475160-83-9P 475160-85-1P 475160-87-3P

475160-88-4P 475160-89-5P 475160-90-8P 475160-91-9P 475160-92-0P  
 475160-93-1P 475160-94-2P 475160-95-3P 475160-96-4P 475160-97-5P  
 475160-98-6P 475160-99-7P 475161-00-3P 475161-01-4P 475161-02-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

IT 537049-40-4P, Tubacin

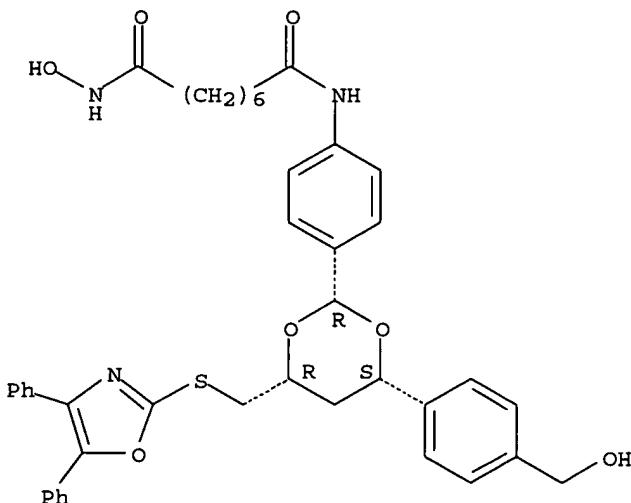
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(claimed compound; preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

RN 537049-40-4 HCPLUS

CN Octanediamide, N-[4-[(2R,4R,6S)-4-[[[4,5-diphenyl-2-oxazolyl]thio]methyl]-6-[(hydroxymethyl)phenyl]-1,3-dioxan-2-yl]phenyl]-N'-hydroxy-, rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.



L38 ANSWER 6 OF 13 HCPLUS COPYRIGHT 2005 ACS on STN

AN 2003:408167 HCPLUS

DN 140:124434

ED Entered STN: 29 May 2003

TI Multidimensional Chemical Genetic Analysis of Diversity-Oriented Synthesis-Derived Deacetylase Inhibitors Using Cell-Based Assays

AU Haggarty, Stephen J.; Koeller, Kathryn M.; Wong, Jason C.; Butcher, Rebecca A.; Schreiber, Stuart L.

CS Departments of Molecular and Cellular Biology, Harvard University, Cambridge, MA, 02138, USA

SO Chemistry & Biology (2003), 10(5), 383-396  
CODEN: CBOLE2; ISSN: 1074-5521

PB Cell Press

DT Journal

LA English

CC 7-3 (Enzymes)

Section cross-reference(s): 9

AB Systematic chemical genetics aims to explore the space representing interactions between small mols. and biol. systems. Beyond measuring binding interactions and enzyme inhibition, measuring changes in the activity of proteins in intact signaling networks is necessary. Toward this end, we are partitioning chemical space into regions with different biol. activities using a panel of cell-based assays and small mol. "chemical genetic modifiers. " Herein, we report on the use of this methodol. for

the discovery of 617 small mol. inhibitors of histone deacetylases from a multidimensional screen of an encoded, diversity-oriented synthesis library. Following decoding of chemical tags and resynthesis, we demonstrate the selectivity of one inhibitory mol. (tubacin) toward  $\alpha$ -tubulin deacetylation and another (histacinc) toward histone deacetylation. These small mols. will facilitate dissecting the role of acetylation in a variety of cell biol. processes.

- ST multidimensional chem genetic analysis deacetylase inhibitor  
 IT Histones  
   RL: BSU (Biological study, unclassified); BIOL (Biological study)  
     (H3; multidimensional chemical genetic anal. of diversity-oriented synthesis-derived deacetylase inhibitors using cell-based assays and selectivity towards  $\alpha$ -tubulin and histone deacetylation)
- IT Histones  
   RL: BSU (Biological study, unclassified); BIOL (Biological study)  
     (H4; multidimensional chemical genetic anal. of diversity-oriented synthesis-derived deacetylase inhibitors using cell-based assays and selectivity towards  $\alpha$ -tubulin and histone deacetylation)
- IT Hydroxamic acids  
   RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
     (functional group of 1,3-dioxane derivs.; multidimensional chemical genetic anal. of diversity-oriented synthesis-derived deacetylase inhibitors using cell-based assays and selectivity towards  $\alpha$ -tubulin and histone deacetylation)
- IT Animal cell  
   (mammalian; multidimensional chemical genetic anal. of diversity-oriented synthesis-derived deacetylase inhibitors using cell-based assays and selectivity towards  $\alpha$ -tubulin and histone deacetylation)
- IT Deacetylation  
   Human  
     Principal component analysis  
       (multidimensional chemical genetic anal. of diversity-oriented synthesis-derived deacetylase inhibitors using cell-based assays and selectivity towards  $\alpha$ -tubulin and histone deacetylation)
- IT Histones  
   RL: BSU (Biological study, unclassified); BIOL (Biological study)  
     (multidimensional chemical genetic anal. of diversity-oriented synthesis-derived deacetylase inhibitors using cell-based assays and selectivity towards  $\alpha$ -tubulin and histone deacetylation)
- IT Tubulins  
   RL: BSU (Biological study, unclassified); BIOL (Biological study)  
     ( $\alpha$ ; multidimensional chemical genetic anal. of diversity-oriented synthesis-derived deacetylase inhibitors using cell-based assays and selectivity towards  $\alpha$ -tubulin and histone deacetylation)
- IT 9025-12-1 9076-57-7, Histone deacetylase 537049-40-4, Tubacin  
 537049-41-5, Histacinc  
   RL: BSU (Biological study, unclassified); BIOL (Biological study)  
     (multidimensional chemical genetic anal. of diversity-oriented synthesis-derived deacetylase inhibitors using cell-based assays and selectivity towards  $\alpha$ -tubulin and histone deacetylation)
- IT 505-22-6D, 1,3-Dioxane, derivs.  
   RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
     (multidimensional chemical genetic anal. of diversity-oriented synthesis-derived deacetylase inhibitors using cell-based assays and selectivity towards  $\alpha$ -tubulin and histone deacetylation)
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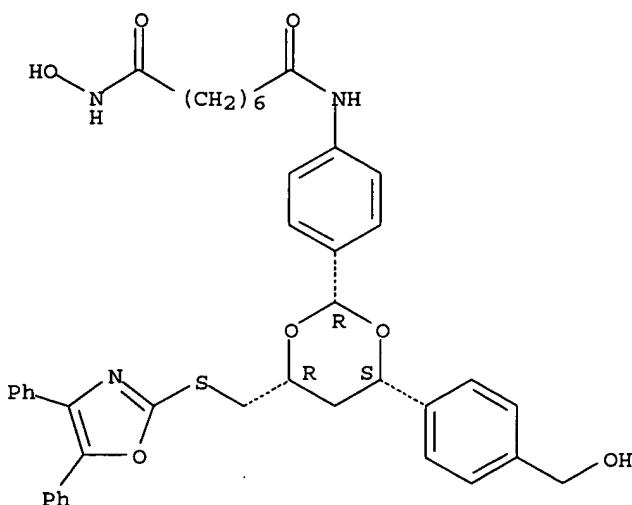
IT 537049-40-4, Tubacin

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (multidimensional chemical genetic anal. of diversity-oriented synthesis-derived deacetylase inhibitors using cell-based assays and selectivity towards  $\alpha$ -tubulin and histone deacetylation)

RN 537049-40-4 HCAPLUS

CN Octanediamide, N-[4-[(2R,4R,6S)-4-[[[(4,5-diphenyl-2-oxazolyl)thio]methyl]-6-[(4-(hydroxymethyl)phenyl]-1,3-dioxan-2-yl]phenyl]-N'-hydroxy-, rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.



L38 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2003:329363 HCAPLUS  
 DN 139:94978  
 ED Entered STN: 30 Apr 2003  
 TI Domain-selective small-molecule inhibitor of histone deacetylase 6  
     (HDAC6)-mediated tubulin deacetylation  
 AU Haggarty, Stephen J.; Koeller, Kathryn M.; Wong, Jason C.;  
     Grozinger, Christina M.; Schreiber, Stuart L.  
 CS Departments of Molecular and Cellular Biology, Harvard  
     University, Cambridge, MA, 02138, USA  
 SO Proceedings of the National Academy of Sciences of the United States of  
     America (2003), 100(8), 4389-4394  
 CODEN: PNASA6; ISSN: 0027-8424  
 PB National Academy of Sciences  
 DT Journal  
 LA English  
 CC 1-6 (Pharmacology)  
 AB Protein acetylation, especially histone acetylation, is the subject of both research and clin. investigation. At least four small-mol. histone deacetylase inhibitors are currently in clin. trials for the treatment of cancer. These and other inhibitors also affect microtubule acetylation. A multidimensional, chemical genetic screen of 7392 small mols. was used to discover "tubacin," which inhibits  $\alpha$ -tubulin deacetylation in mammalian cells. Tubacin does not affect the level of histone acetylation, gene-expression patterns, or cell-cycle progression. We provide evidence that class II histone deacetylase 6 (HDAC6) is the intracellular target of tubacin. Only one of the two catalytic domains of HDAC6 possesses tubulin deacetylase activity, and only this domain is bound by tubacin. Tubacin treatment did not affect the stability of microtubules but did decrease cell motility. HDAC6 overexpression disrupted the localization of p58, a protein that mediates binding of Golgi elements to microtubules. Our results highlight the role of  $\alpha$ -tubulin acetylation in mediating the localization of microtubule-associated proteins. They also suggest that small mols. that selectively inhibit HDAC6-mediated  $\alpha$ -tubulin deacetylation, a first example of which is tubacin, might have therapeutic applications as antimetastatic and antiangiogenic agents.  
 ST histone deacetylase tubacin niltubacin human antitumor  
 IT Proteins  
     RL: BSU (Biological study, unclassified); BIOL (Biological study)  
         (MAP (microtubule-associated protein); domain-selective small-mol.  
         inhibitor of histone deacetylase 6 (HDAC6)-mediated tubulin  
         deacetylation)  
 IT Proteins  
     RL: BSU (Biological study, unclassified); BIOL (Biological study)  
         (P58; domain-selective small-mol. inhibitor of histone deacetylase 6  
         (HDAC6)-mediated tubulin deacetylation)  
 IT Angiogenesis inhibitors  
     Antitumor agents  
     Cell cycle  
     Drug screening  
     Enzyme functional sites  
     Human  
         (domain-selective small-mol. inhibitor of histone deacetylase 6  
         (HDAC6)-mediated tubulin deacetylation)  
 IT Tubulins  
     RL: BSU (Biological study, unclassified); BIOL (Biological study)  
         (domain-selective small-mol. inhibitor of histone deacetylase 6  
         (HDAC6)-mediated tubulin deacetylation)  
 IT Gene  
     RL: BSU (Biological study, unclassified); BIOL (Biological study)  
         (expression; domain-selective small-mol. inhibitor of histone  
         deacetylase 6 (HDAC6)-mediated tubulin deacetylation)  
 IT 9076-57-7, Histone deacetylase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (domain-selective small-mol. inhibitor of histone deacetylase 6  
 (HDAC6)-mediated tubulin deacetylation)

IT 537049-40-4, Tubacin 560102-50-3, Niltubacin  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (domain-selective small-mol. inhibitor of histone deacetylase 6  
 (HDAC6)-mediated tubulin deacetylation)

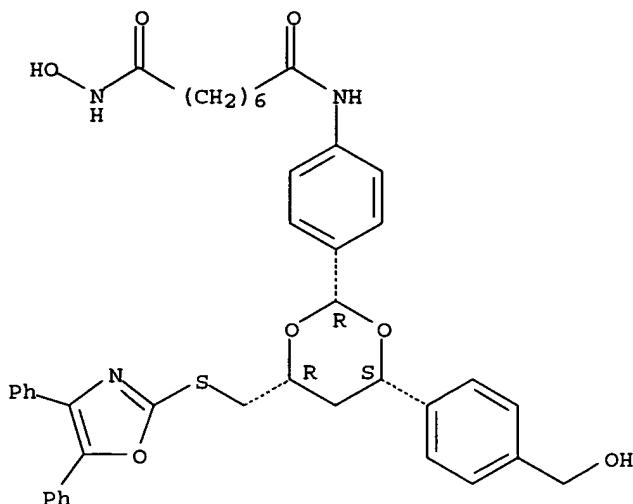
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 RE

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IT 537049-40-4, Tubacin  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (domain-selective small-mol. inhibitor of histone deacetylase 6  
 (HDAC6)-mediated tubulin deacetylation)

RN 537049-40-4 HCPLUS  
 CN Octanediamide, N-[4-[(2R,4R,6S)-4-[[[(4,5-diphenyl-2-oxazolyl)thio]methyl]-6-[4-(hydroxymethyl)phenyl]-1,3-dioxan-2-yl]phenyl]-N'-hydroxy-, rel-  
 (9CI) (CA INDEX NAME)

Relative stereochemistry.



L38 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2003:292422 HCAPLUS  
 DN 139:17111  
 ED Entered STN: 16 Apr 2003  
 TI Structural Biasing Elements for In-Cell Histone Deacetylase Paralog Selectivity  
 AU Wong, Jason C.; Hong, Roger; Schreiber, Stuart L.  
 CS Department of Chemistry and Chemical Biology Harvard Institute of Chemistry and Cell Biology, Howard Hughes Medical Institute, Harvard University, Cambridge, MA, 02138, USA  
 SO Journal of the American Chemical Society (2003), 125(19), 5586-5587  
 CODEN: JACSAT; ISSN: 0002-7863  
 PB American Chemical Society  
 DT Journal  
 LA English  
 CC 1-3 (Pharmacology)  
 AB We use the structural dissection of two 1,3-dioxanes with in-cell histone deacetylase (HDAC) paralog selectivity to identify key elements for selective HDAC inhibitors. We demonstrate that o-aminoanilides are inactive toward HDAC6 while apparently inhibiting deacetylases that act upon histone substrates. This finding has important clin. implications for the development of HDAC inhibitor-based treatments that do not interfere with microtubule dynamics associated with HDAC6. We also show that suberoylanilide hydroxamic acid (SAHA) alone is a nonparalog-selective HDAC inhibitor and that the 1,3-dioxane diversity appended to SAHA is essential for HDAC6 paralog selectivity.  
 ST structure activity relationship biasing element histone deacetylase paralog design  
 IT Structure-activity relationship (enzyme-inhibiting; structural biasing elements for In-cell histone deacetylase paralog selectivity)  
 IT 9076-57-7, Histone deacetylase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (structural biasing elements for In-cell histone deacetylase paralog selectivity)  
 IT 58880-19-6, Trichostatin A 133155-90-5, Trapoxin B 149647-78-9, Suberoylanilide hydroxamic acid 537034-14-3 537034-15-4 537034-16-5 537034-17-6 537049-40-4, Tubacin 537049-41-5, Histacin  
 RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (structural biasing elements for In-cell histone deacetylase paralog selectivity)

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD  
RE

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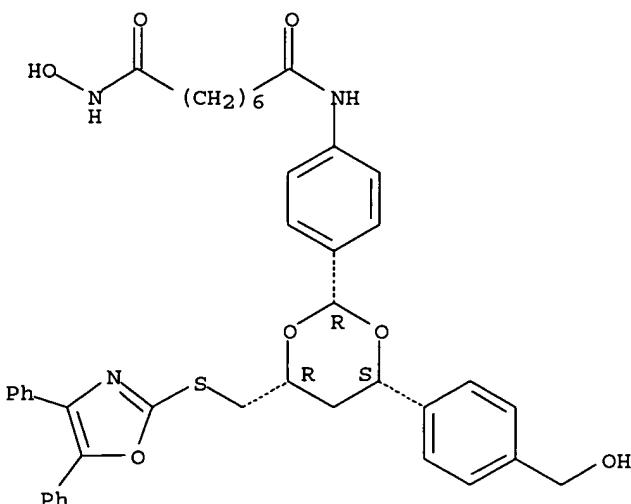
IT 537049-40-4, Tubacin

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(structural biasing elements for In-cell histone deacetylase paralog selectivity)

RN 537049-40-4 HCAPLUS

CN Octanediamide, N-[4-[(2R,4R,6S)-4-[[{(4,5-diphenyl-2-oxazolyl)thio]methyl]-6-[4-(hydroxymethyl)phenyl]-1,3-dioxan-2-yl]phenyl]-N'-hydroxy-, rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.



L38 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:868720 HCAPLUS

DN 137:370095

ED Entered STN: 15 Nov 2002

TI Preparation of dioxanes as inhibitors of histone deacetylase.

IN Schreiber, Stuart L.; Sternson, Scott M.; Wong, Jason C.; Grozinger, Christina M.

PA President & Fellows of Harvard College, USA

SO PCT Int. Appl., 119 pp.

CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K031-00  
 ICS C07D319-06; C07D417-12; C07D413-12; C07D493-10; A61P035-00  
 CC 28-11 (Heterocyclic Compounds (More Than One Hetero Atom))  
 Section cross-reference(s): 1, 26

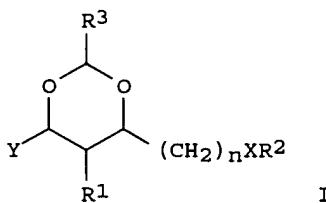
## FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002089782	A2	20021114	WO 2002-US14835	20020509 <--
	WO 2002089782	A3	20030227		
		W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
		RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG		
PRAI US	2001-289850P	P	20010509	<--	

## CLASS

	PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
	WO 2002089782	ICM	A61K031-00
		ICS	C07D319-06; C07D417-12; C07D413-12; C07D493-10; A61P035-00
	WO 2002089782	ECLA	C07D319/06; C07D405/06+319+211; C07D405/12+319+257; C07D413/12+319+263B; C07D417/12+319+277; C07D491/10+317A+221A
			<--

OS MARPAT 137:370095  
 GI



AB Title compds. [I; R1 = H, (substituted) aliphatyl, heteroaliphatyl, aryl, heteroaryl, etc.; n = 1-5; R2 = H, protecting group, (substituted) aliphatyl, heteroaliphatyl, aryl, heteroaryl, etc.; X = O, S, (substituted) CH<sub>2</sub>, imino; R3 = (substituted) aliphatyl, heteroaliphatyl, aryl, heteroaryl, etc.; Y = H, aliphatyl, heteroaliphatyl, aryl, heteroaryl, etc.], were prepared. Thus, (αS)-2-acetoxy-N-[(4-[(4S,6R)-4-[[[(4,5-diphenyl-2-oxazolyl)thio]methyl]-6-[4-(hydroxymethyl)phenyl]-1,3-dioxan-2-yl]phenyl)methyl]propionamide (solid phase preparation given) inhibited HDAC1 and HDAC6 with IC<sub>50</sub>'s of about 1 μM. The present invention addnl. provides methods for modulating the glucose-sensitive subset of genes downstream of Ure2p.

ST dioxane prep histone deacetylase inhibitor; HDAC1 HDAC6 inhibitor dioxane prep; uretupamine analog prep anticancer

IT Antitumor agents  
 Combinatorial library

Human

Solid phase synthesis

(preparation of dioxanes as inhibitors of histone deacetylase)

IT Neoplasm

(treatment; preparation of dioxanes as inhibitors of histone deacetylase)

IT 9076-57-7, Histone deacetylase 134773-68-5, Protein (Saccharomyces cerevisiae clone p1I-Bs gene URE2)  
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; preparation of dioxanes as inhibitors of histone deacetylase)

IT 475160-81-7P 475160-82-8P  
 RL: ANT (Analyte); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation) (preparation of dioxanes as inhibitors of histone deacetylase)

IT 475161-07-0P 475161-08-1P  
 RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent) (preparation of dioxanes as inhibitors of histone deacetylase)

IT 332925-19-6P 332925-20-9P 332925-21-0P 394657-68-2P  
 475161-03-6P 475161-04-7P 475161-05-8P  
 475161-06-9P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of dioxanes as inhibitors of histone deacetylase)

IT 56-91-7, 4-(Aminomethyl)benzoic acid 505-48-6, Suberic acid 589-29-7, 1,4-Benzenedimethanol 623-04-1, 4-Aminobenzyl alcohol 873-75-6, 4-Bromobenzyl alcohol 1877-77-6, 3-Aminobenzyl alcohol 17564-64-6, Chloromethylphthalimide 20445-31-2, (R)-MTPA 38002-45-8, 3-Trimethylsilylpropargyl bromide 39959-54-1, 3-Bromobenzylamine hydrochloride 87199-16-4, 3-Formylphenylboronic acid 87199-17-5, 4-Formylphenylboronic acid  
 RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of dioxanes as inhibitors of histone deacetylase)

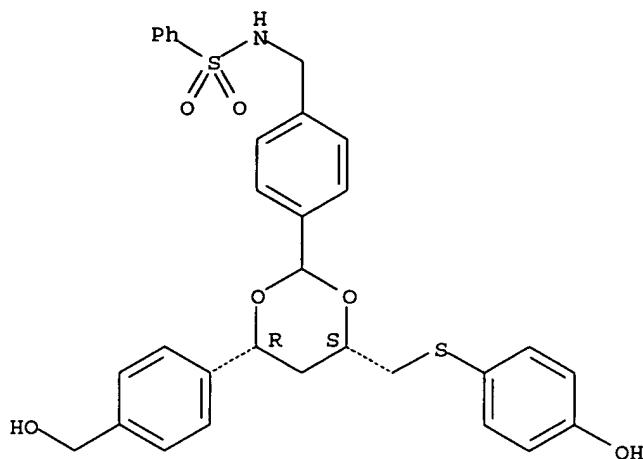
IT 146952-73-0P 164470-64-8P 196880-47-4P 206537-33-9P 206537-34-0P  
 332925-17-4P 475160-70-4P 475160-73-7P 475160-74-8P 475160-75-9P  
 475160-76-0P 475160-77-1P 475160-78-2P 475160-79-3P 475160-80-6P  
 475160-83-9P 475160-85-1P 475160-87-3P 475160-88-4P 475160-89-5P  
 475160-90-8P 475160-91-9P 475160-92-0P 475160-93-1P 475160-94-2P  
 475160-95-3P 475160-96-4P 475160-97-5P 475160-98-6P 475160-99-7P  
 475161-00-3P 475161-01-4P 475161-02-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of dioxanes as inhibitors of histone deacetylase)

IT 332925-20-9P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of dioxanes as inhibitors of histone deacetylase)

RN 332925-20-9 HCPLUS

CN Benzenesulfonamide, N-[[4-[(4R,6S)-4-[4-(hydroxymethyl)phenyl]-6-[[[(4-hydroxyphenyl)thio]methyl]-1,3-dioxan-2-yl]phenyl]methyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L38 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2002:312569 HCAPLUS  
 DN 137:75366  
 ED Entered STN: 26 Apr 2002  
 TI Dissecting glucose signalling with diversity-oriented synthesis and small-molecule microarrays  
 AU Kuruvilla, Finny G.; Shamji, Alykhan F.; Sternson, Scott M.; Hergenrother, Paul J.; Schreiber, Stuart L.  
 CS Howard Hughes Medical Institute, Institute for Chemistry and Cell Biology, Bauer Center for Genomics Research, Department of Chemistry and Chemical Biology, Harvard University, Cambridge, MA, 02138, USA  
 SO Nature (London, United Kingdom) (2002), 416(6881), 653-657  
 CODEN: NATUAS; ISSN: 0028-0836  
 PB Nature Publishing Group  
 DT Journal  
 LA English  
 CC 9-2 (Biochemical Methods)  
 AB Small mols. that alter protein function provide a means to modulate biol. networks with temporal resolution. Here the authors demonstrate a potentially general and scalable method of identifying such mols. by application to a particular protein, Ure2p, which represses the transcription factors Gln3p and Nillp. By probing a high-d. microarray of small mols. generated by diversity-oriented synthesis with fluorescently labeled Ure2p, the authors performed 3780 protein-binding assays in parallel and identified several compds. that bind Ure2p. One compound, which the authors call uretupamine, specifically activates a glucose-sensitive transcriptional pathway downstream of Ure2p. Whole-genome transcription profiling and chemical epistasis demonstrate the remarkable Ure2p specificity of uretupamine and its ability to modulate the glucose-sensitive subset of genes downstream of Ure2p. These results demonstrate that diversity-oriented synthesis and small-mol. microarrays can be used to identify small mols. that bind to a protein of interest, and that these small mols. can regulate specific functions of the protein.  
 ST uretupamine binding protein Ure2p signal analysis  
 IT Signal transduction, biological  
 Transcription, genetic  
 (dissecting glucose signalling with diversity-oriented synthesis and small-mol. microarrays)  
 IT Proteins  
 RL: BCP (Biochemical process); BIOL (Biological study); PROC (Process)  
 (gene URE2; dissecting glucose signalling with diversity-oriented synthesis and small-mol. microarrays)  
 IT 441063-83-8, Uretupamine A 441063-84-9, Uretupamine B

441063-85-0, Uretupamine C 441063-86-1, Uretupamine D  
 441063-87-2, Uretupamine E 441063-88-3, Uretupamine F  
 441063-89-4, Uretupamine G 441063-90-7, Uretupamine H  
 RL: ARG (Analytical reagent use); BSU (Biological study, unclassified);  
 ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (dissecting glucose signalling with diversity-oriented synthesis and  
 small-mol. microarrays)

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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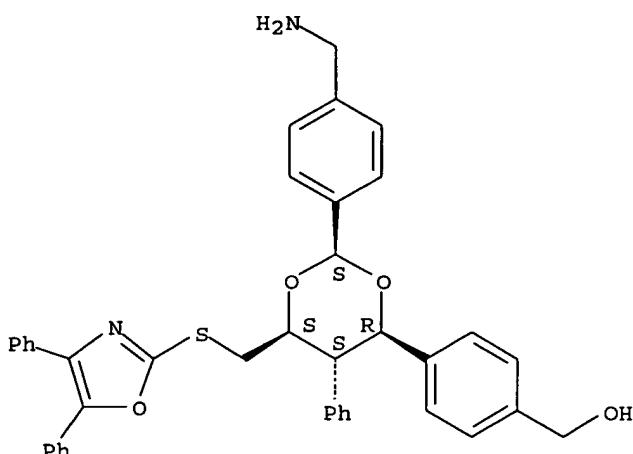
IT 441063-83-8, Uretupamine A

RL: ARG (Analytical reagent use); BSU (Biological study, unclassified);  
 ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (dissecting glucose signalling with diversity-oriented synthesis and  
 small-mol. microarrays)

RN 441063-83-8 HCPLUS

CN Benzenemethanol, 4-[(2R,4S,5R,6R)-2-[4-(aminomethyl)phenyl]-6-[[[(4,5-diphenyl-2-oxazolyl)thio]methyl]-5-phenyl-1,3-dioxan-4-yl]-, rel- (9CI)  
 (CA INDEX NAME)

Relative stereochemistry.



L38 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2001:864080 HCAPLUS  
 DN 136:144662  
 ED Entered STN: 30 Nov 2001  
 TI Synthesis of 7200 Small Molecules Based on a Substructural Analysis of the Histone Deacetylase Inhibitors Trichostatin and Trapoxin  
 AU Sternson, Scott M.; Wong, Jason C.; Grozinger, Christina M.; Schreiber, Stuart L.  
 CS Howard Hughes Medical Institute Institute of Chemistry and Cell Biology Department of Chemistry Chemical Biology, Harvard University, Cambridge, MA, 02138, USA  
 SO Organic Letters (2001), 3(26), 4239-4242  
 CODEN: ORLEF7; ISSN: 1523-7060  
 PB American Chemical Society  
 DT Journal  
 LA English  
 CC 1-3 (Pharmacology)  
 AB Seventy-two hundred potential inhibitors of the histone deacetylase (HDAC) enzyme family, based on a 1,3-dioxane diversity structure, were synthesized on polystyrene macrobeads. The compds. were arrayed for biol. assays in a "one bead-one stock solution" format. Metal-chelating functional groups were used to direct the 1,3-dioxanes to HDAC enzymes, which are zinc hydrolases. Representative structures from this library were tested for inhibitory activity and the 1,3-dioxane structure was shown to be compatible with HDAC inhibition.  
 ST histone deacetylase inhibitor trichostatin trapoxin structure; antitumor dioxane deriv prepn SAR  
 IT Antitumor agents  
 Structure-activity relationship  
 (synthesis of 7200 small mols. based on a substructural anal. of histone deacetylase inhibitors trichostatin and trapoxin)  
 IT 9076-57-7, Histone deacetylase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (synthesis of 7200 small mols. based on a substructural anal. of histone deacetylase inhibitors trichostatin and trapoxin)  
 IT 58880-19-6, Trichostatin A 133155-89-2 394657-68-2  
 394657-69-3 394657-70-6  
 RL: PAC (Pharmacological activity); BIOL (Biological study)  
 (synthesis of 7200 small mols. based on a substructural anal. of histone deacetylase inhibitors trichostatin and trapoxin)  
 RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 RE  
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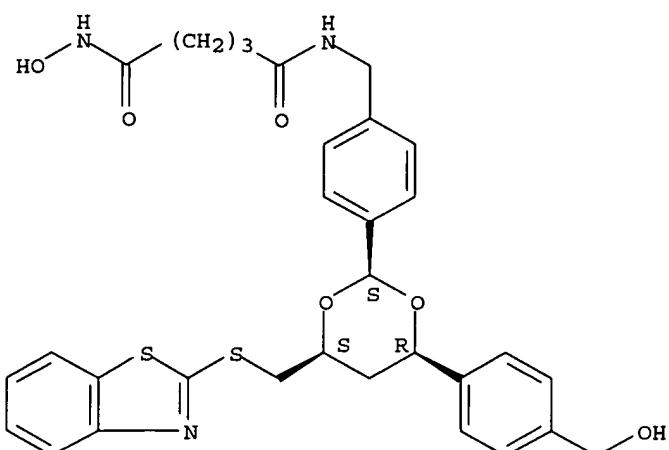
IT 394657-68-2

RL: PAC (Pharmacological activity); BIOL (Biological study)  
 (synthesis of 7200 small mols. based on a substructural anal. of  
 histone deacetylase inhibitors trichostatin and trapoxin)

RN 394657-68-2 HCAPLUS

CN Pentanediamide, N-[(4-[(2R,4R,6S)-4-[(2-benzothiazolylthio)methyl]-6-[4-(hydroxymethyl)phenyl]-1,3-dioxan-2-yl]phenyl)methyl]-N'-hydroxy-, rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.



L38 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:68706 HCAPLUS

DN 134:280788

ED Entered STN: 31 Jan 2001

TI Split-Pool Synthesis of 1,3-Dioxanes Leading to Arrayed Stock Solutions of Single Compounds Sufficient for Multiple Phenotypic and Protein-Binding Assays

AU Sternson, Scott M.; Louca, Joseph B.; Wong, Jason C.; Schreiber, Stuart L.

CS Harvard Institute of Chemistry and Cell Biology, Harvard Medical School, Boston, MA, 02115, USA

SO Journal of the American Chemical Society (2001), 123(8), 1740-1747

PB CODEN: JACSAT; ISSN: 0002-7863  
 DT American Chemical Society  
 LA Journal  
 English  
 CC 28-11 (Heterocyclic Compounds (More Than One Hetero Atom))  
 Section cross-reference(s): 9  
 OS CASREACT 134:280788  
 AB Diversity-oriented organic synthesis offers the promise of advancing chemical genetics, where small mols. are used to explore biol. While the split-pool synthetic method is theor. the most effective approach for the production of large collections of small mols., it has not been widely adopted due to numerous tech. and anal. hurdles. The authors have developed a split-pool synthesis leading to an array of stock solns. of single 1,3-dioxanes. The quantities of compds. are sufficient for hundreds of phenotypic and protein-binding assays. The average concentration of these stock solns. derived from a single synthesis bead was determined to be 5.4 mM in 5 µL of DMSO. A mass spectrometric strategy to identify the structure of mols. from a split-pool synthesis was shown to be highly accurate. Individual members of the 1,3-dioxane library have activity in a variety of phenotypic and protein-binding assays. The procedure developed in this study allows many assays to be performed with compds. derived from individual synthesis beads. The synthetic compds. identified in these assays should serve as useful probes of cellular and organismal processes.  
 ST split pool synthesis dioxane; multiple phenotypic protein binding assay  
 dioxane  
 IT Phenotypes  
 (split-pool synthesis of 1,3-dioxanes leading to arrayed stock solns. of single compds. sufficient for multiple phenotypic and protein-binding assays)  
 IT Proteins, general, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (split-pool synthesis of 1,3-dioxanes leading to arrayed stock solns. of single compds. sufficient for multiple phenotypic and protein-binding assays)  
 IT 332925-18-5P 332925-19-6P 332925-20-9P 332925-21-0P  
 333326-20-8P 333326-22-0P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (split-pool synthesis of 1,3-dioxanes leading to arrayed stock solns. of single compds. sufficient for multiple phenotypic and protein-binding assays)  
 IT 177-11-7, 1,4-Dioxa-8-azaspiro[4.5]decane 637-89-8 1121-31-9  
 6670-13-9 13183-79-4 29739-88-6 36394-75-9 63638-93-7  
 332925-17-4 475160-87-3 475160-91-9 681219-14-7 681221-63-6  
 681225-91-2  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (split-pool synthesis of 1,3-dioxanes leading to arrayed stock solns. of single compds. sufficient for multiple phenotypic and protein-binding assays)  
 IT 332925-16-3DP, resin bound  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (split-pool synthesis of 1,3-dioxanes leading to arrayed stock solns. of single compds. sufficient for multiple phenotypic and protein-binding assays)  
 RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 RE  
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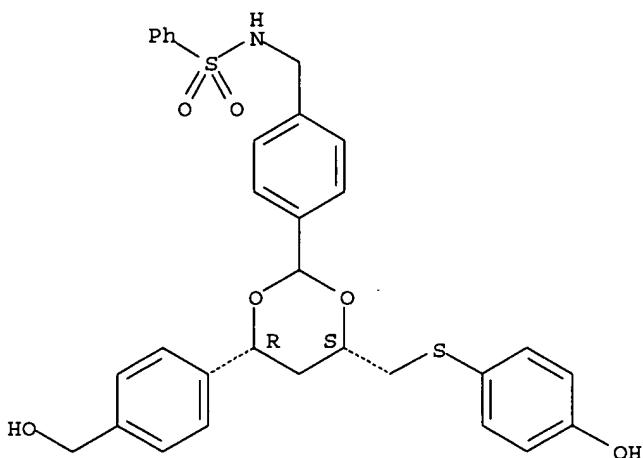
IT 332925-20-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (split-pool synthesis of 1,3-dioxanes leading to arrayed stock solns.  
 of single compds. sufficient for multiple phenotypic and  
 protein-binding assays)

RN 332925-20-9 HCAPLUS

CN Benzenesulfonamide, N-[[4-[(4R,6S)-4-[4-(hydroxymethyl)phenyl]-6-[[[4-hydroxyphenyl]thio]methyl]-1,3-dioxan-2-yl]phenyl]methyl]-, rel- (9CI)  
 (CA INDEX NAME)

Relative stereochemistry.



L38 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:251317 HCAPLUS

DN 128:319046

ED Entered STN: 02 May 1998

TI Droplet assay system for screening combinatorial libraries  
 IN Schreiber, Stuart L.; Shair, Matthew D.; Borchardt, Allen J.;  
 You, Angie J.; Huang, Jing; Foley, Mike; Tan, Derek; Whitesides, George;  
 Jackman, Rebecca J.

PA President and Fellows of Harvard College, USA  
 SO PCT Int. Appl., 126 pp.  
 CODEN: PIXXD2

DT Patent

LA English

IC ICM G01N033-53

CC 9-1 (Biochemical Methods)

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9816830	A2	19980423	WO 1997-US19110	19971015
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9852391	A1	19980511	AU 1998-52391	19971015
PRAI	US 1996-29128P	P	19961016		
	US 1997-49864P	P	19970606		
	WO 1997-US19110	W	19971015		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9816830	ICM	G01N033-53
WO 9816830	ECLA	B01J019/00C; G01N033/50

AB The present invention provides a novel system for simultaneously screening a large number of compds. and identifying compds. having desirable chemical or biol. activities. According to the invention, test compds. are isolated in and introduced into liquid droplets within which their activities are studied. Multiple droplets are displayed simultaneously on a single surface without risk of confusion because the sep. identity of each droplet is maintained and diffusion of test compds. from one droplet to another is avoided. In certain embodiments, these goals are accomplished through reliance on droplet surface tension. In other embodiments, the droplets are localized in micro-wells that retain droplet integrity. The system is particularly useful for identifying compds. that act e.g., as catalysts, or that have biol. activities. In preferred embodiments of the invention, the compds. are assayed *in vivo*.

ST combinatorial library droplet assay system; droplet assay app

IT Combinatorial library

(droplet assay system for simultaneously assaying combinatorial libraries and identifying compds. of chemical or biol. activities)

IT Bioassay

(droplet; droplet assay system for simultaneously screening combinatorial libraries and identifying compds. of chemical or biol. activities)

IT 65-85-0, Benzoic acid, reactions 79-22-1, Methyl chloroformate  
 99-05-8, 3-Aminobenzoic acid 100-51-6, Benzyl alcohol, reactions  
 103-71-9, Phenyl isocyanate, reactions 103-80-0, Phenylacetyl chloride  
 108-31-6, 2,5-Furandione, reactions 109-73-9, Butylamine, reactions  
 109-85-3, (2-Methoxyethyl)amine 109-89-7, Diethylamine, reactions  
 110-89-4, Piperidine, reactions 123-62-6, Propionic anhydride  
 141-82-2, Malonic acid, reactions 552-89-6, 2-Nitrobenzaldehyde  
 563-96-2, Glyoxylic acid monohydrate 619-66-9, 4-Carboxybenzaldehyde  
 631-61-8, Ammonium acetate 636-98-6, 1-Iodo-4-nitrobenzene 922-68-9,  
 Methyl glyoxylate 924-44-7, Ethyl glyoxylate 1711-02-0, 4-Iodobenzoyl  
 chloride 1877-77-6, 3-Aminobenzyl alcohol 5416-93-3, 4-Methoxyphenyl  
 isocyanate 5470-11-1, Hydroxylamine hydrochloride 24424-99-5,  
 Di-tert-butyl dicarbonate 24850-33-7, Allyltributyltin 39178-35-3,

Isonicotinoyl chloride hydrochloride 76985-84-7 81863-45-8,  
 3-Amino-4-methylbenzyl alcohol 82911-69-1 88574-06-5,  
 6-(9-Fluorenylmethoxycarbonylamino)hexanoic acid 104987-11-3  
 113928-90-8, 3-Amino-4-methoxybenzyl alcohol 141565-14-2 206537-46-4D,  
 resin-bound

RL: RCT (Reactant); RACT (Reactant or reagent)

(droplet assay system for simultaneously assaying combinatorial  
 libraries and identifying compds. of chemical or biol. activities)

IT 1453-82-3DP, 4-Carbamoylpyridine, TGR-ANP-ACA resin-bound 5678-48-8P  
 14454-14-9P, N-(4-Iodophenyl)hydroxylamine 15164-44-0P,  
 4-Iodobenzaldehyde 78767-55-2P 83670-49-9P, N-(4-  
 Bromobenzyl)hydroxylamine 88574-06-5DP, ANP resin-bound 206537-10-2DP,  
 resin-bound 206537-15-7P 206537-16-8P 206537-17-9DP, ANP-TGR  
 resin-bound 206537-18-0DP, ANP-TGR resin-bound 206537-19-1DP, ANP-TGR  
 resin-bound 206537-20-4DP, ANP-TGR resin-bound 206537-21-5DP,  
 resin-bound 206537-21-5P 206537-23-7P, N-(4-Iodobenzyl)hydroxylamine  
 206537-24-8P 206537-25-9P 206537-26-0P 206537-27-1P 206537-28-2DP,  
 Tentagel-bound 206537-28-2P 206537-29-3P 206537-30-6P 206537-31-7P  
 206537-32-8P 206537-33-9P 206537-34-0P 206537-35-1P 206537-36-2P  
 206537-37-3P 206537-38-4P 206537-39-5P 206537-40-8P 206537-41-9DP,  
 TGR-ANP-ACA resin-bound 206537-42-0DP, TGR-ANP-ACA resin-bound  
 206537-43-1DP, TGR-ANP-ACA resin-bound

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)

(droplet assay system for simultaneously assaying combinatorial  
 libraries and identifying compds. of chemical or biol. activities)

IT 206537-10-2P 206537-11-3P 206537-12-4P 206537-13-5DP,  
 resin-bound 206537-14-6DP, resin-bound 206537-22-6P 206537-44-2DP,  
 resin-bound 206537-45-3DP, resin-bound 206537-47-5P 206537-48-6DP,  
 resin-bound

RL: SPN (Synthetic preparation); PREP (Preparation)

(droplet assay system for simultaneously assaying combinatorial  
 libraries and identifying compds. of chemical or biol. activities)

IT 206537-12-4P

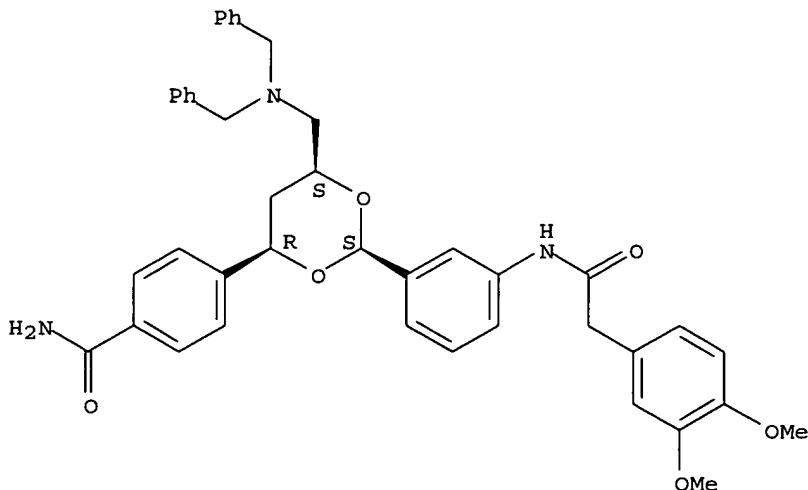
RL: SPN (Synthetic preparation); PREP (Preparation)

(droplet assay system for simultaneously assaying combinatorial  
 libraries and identifying compds. of chemical or biol. activities)

RN 206537-12-4 HCPLUS

CN Benzeneacetamide, N-[3-[(2S,4R,6S)-4-[4-(aminocarbonyl)phenyl]-6-  
 [[bis(phenylmethyl)amino]methyl]-1,3-dioxan-2-yl]phenyl]-3,4-dimethoxy-  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d all hitstr 146 tot

L46 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2001:764368 HCAPLUS  
 DN 136:69857  
 ED Entered STN: 21 Oct 2001  
 TI Acid-catalyzed cyclization of vinylsilanes bearing a hemiacetal group  
 AU Miura, Katsukiyo; Takahashi, Tatsuyuki; Nishikori, Hisashi; Hosomi, Akira  
 CS Department of Chemistry, Graduate School of Pure and Applied Sciences,  
 University of Tsukuba, Tsukuba, 305-8571, Japan  
 SO Chemistry Letters (2001), (10), 958-959  
 CODEN: CMLTAG; ISSN: 0366-7022  
 PB Chemical Society of Japan  
 DT Journal  
 LA English  
 CC 29-6 (Organometallic and Organometalloidal Compounds)  
 Section cross-reference(s): 28  
 OS CASREACT 136:69857  
 AB In the presence of a catalytic amount of  $TsOH \cdot H_2O$ , hemiacetals derived from (Z)-4-trialkylsilyl-3-buten-1-ols and chloral were cyclized to 2-trichloromethyl-4-trialkylsilylmethyl-1,3-dioxanes in good to high yields. The substrates bearing an allylic substituent achieved high levels of 1,2-asym. induction. When the silyl group was a benzyldimethylsilyl group, the products could be efficiently converted to 1,2,4-triol derivs. by oxidative cleavage of the silicon-carbon bond.  
 ST acid catalyzed cyclization vinylsilane hemiacetal group; silyl butenol acid catalyzed cyclization; chloromethyl trialkylsilylmethyl dioxane prepn oxidative cleavage  
 IT Cyclization  
 Cyclization catalysts  
 (acid-catalyzed cyclization of vinylsilanes bearing a hemiacetal group)  
 IT Acetals  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (hemiacetals; acid-catalyzed cyclization of vinylsilanes bearing a hemiacetal group)  
 IT 75-87-6, Chloral 78-84-2, Isopropylcarboxaldehyde 100-52-7, Benzaldehyde, reactions 123-11-5, 4-Methoxybenzaldehyde, reactions 555-16-8, 4-Nitrobenzaldehyde, reactions  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (acid-catalyzed cyclization of vinylsilanes bearing hemiacetal group with)  
 IT 385372-66-7 385372-67-8 385372-68-9 385372-69-0 385372-70-3  
 385372-71-4 385372-72-5 385372-73-6 385372-74-7  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (acid-catalyzed cyclization of vinylsilanes bearing hemiacetal group with chloral)  
 IT 154673-67-3 385372-65-6  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (acid-catalyzed cyclization of with chloral)  
 IT 385372-75-8P 385372-77-0P 385372-79-2P 385372-81-6P 385372-83-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and desilylation of)  
 IT 385372-76-9P 385372-78-1P 385372-80-5P 385372-82-7P 385372-84-9P  
 385372-85-0P 385372-86-1P 385372-87-2P 385372-88-3P  
 385372-89-4P 385372-90-7P 385372-91-8P 385372-92-9P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD

- RE  
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 (2) Anon; Studies on Organosilicon Chemistry 154  
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- (5) Fleming, I; Chemtracts: Organic Chemistry 1996, V9, P1 HCAPLUS  
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 (23) Yang, X; J Org Chem 2001, V66, P739 HCAPLUS

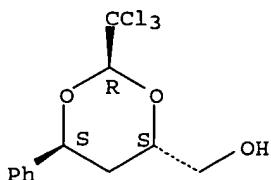
IT 385372-89-4P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RN 385372-89-4 HCAPLUS

CN 1,3-Dioxane-4-methanol, 6-phenyl-2-(trichloromethyl)-, (2R,4S,6S)-rel-  
(9CI) (CA INDEX NAME)

Relative stereochemistry.



L46 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:156170 HCAPLUS

DN 134:340467

ED Entered STN: 06 Mar 2001

TI An enantioselective synthesis of benzylidene-protected syn-3,5-dihydroxy carboxylate esters via osmium, palladium, and base catalysis

AU Hunter, Thomas J.; O'Doherty, George A.

CS Department of Chemistry, University of Minnesota, Minneapolis, MN, 55455, USA

SO Organic Letters (2001), 3(7), 1049-1052  
CODEN: ORLEF7; ISSN: 1523-7060

PB American Chemical Society

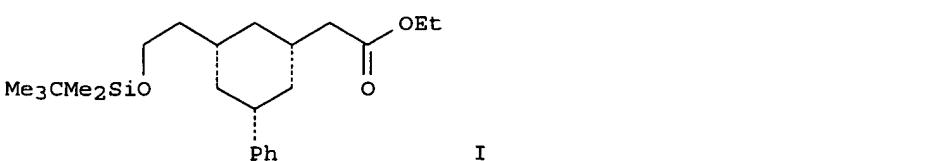
DT Journal

LA English

CC 28-11 (Heterocyclic Compounds (More Than One Hetero Atom))

OS CASREACT 134:340467

GI



- AB The enantioselective syntheses of several protected *syn*-3,5-dihydroxy carboxylic esters, e.g. I, have been achieved from the corresponding achiral 1,3-dieneoates, e.g. Me<sub>3</sub>CsiMe<sub>2</sub>OCH<sub>2</sub>CH:CHCH:CHCO<sub>2</sub>Et. The route relies upon an enantio- and regioselective Sharpless dihydroxylation and a palladium-catalyzed reduction to form  $\delta$ -hydroxy-1-enoates, e.g. (S)-Me<sub>3</sub>CMe<sub>2</sub>SiOCH<sub>2</sub>CH(OH)CH<sub>2</sub>CH:CHCO<sub>2</sub>Et. The resulting  $\delta$ -hydroxy-1-enoates are subsequently converted into benzylidene-protected 3,5-dihydroxy carboxylic esters in one step. The benzylidene-protected 3,5-dihydroxy carboxylic esters are produced in good overall yields (25% to 51%) and high enantiomeric excesses (80% to >95%).
- ST enantioselective synthesis benzylidene dihydroxy carboxylate ester;
- IT palladium enantioselective synthesis benzylidene carboxylate ester
- IT Asymmetric synthesis and induction
- Reduction
- Reduction catalysts
- Stereochemistry
- (asym. synthesis of benzylidene-dihydroxy carboxylates via enantio- and regioselective Sharpless dihydroxylation and palladium-catalyzed reduction)
- IT Esters, preparation
- RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
- (asym. synthesis of benzylidene-dihydroxy carboxylates via enantio- and regioselective Sharpless dihydroxylation and palladium-catalyzed reduction)
- IT Hydroxylation
- (stereoselective, di-, Sharpless, regioselective; asym. synthesis of benzylidene-dihydroxy carboxylates via enantio- and regioselective Sharpless dihydroxylation and palladium-catalyzed reduction)
- IT 100-52-7, Benzaldehyde, reactions 541-41-3, Ethyl chloroformate  
115349-62-7 120310-01-2 337508-92-6
- RL: RCT (Reactant); RACT (Reactant or reagent)
- (asym. synthesis of benzylidene-dihydroxy carboxylates via enantio- and regioselective Sharpless dihydroxylation and palladium-catalyzed reduction)
- IT 2396-84-1P 39806-16-1P 74418-28-3P 198009-56-2P 337508-75-5P  
337508-76-6P 337508-77-7P 337508-78-8P 337508-79-9P 337508-86-8P  
337508-87-9P
- RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
- (asym. synthesis of benzylidene-dihydroxy carboxylates via enantio- and regioselective Sharpless dihydroxylation and palladium-catalyzed reduction)
- IT 188924-78-9P 188924-79-0P 337508-80-2P 337508-81-3P 337508-82-4P  
337508-83-5P 337508-84-6P 337508-85-7P 337508-88-0P  
337508-89-1P 337508-90-4P 337508-91-5P 337508-93-7P 337508-94-8P  
337508-95-9P 337508-96-0P 337508-97-1P 337508-98-2P 337508-99-3P
- RL: SPN (Synthetic preparation); PREP (Preparation)
- (asym. synthesis of benzylidene-dihydroxy carboxylates via enantio- and regioselective Sharpless dihydroxylation and palladium-catalyzed reduction)
- IT 32315-10-9, Triphosgene 89238-99-3, 4-Methoxybenzyl trichloroacetimidate
- RL: RCT (Reactant); RACT (Reactant or reagent)
- (preparation of)
- IT 140853-10-7
- RL: RGT (Reagent); RACT (Reactant or reagent)
- (preparation of)
- RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
- RE
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  - (2) Ambrosio, M; Helv Chim Acta 1996, V79, P51
  - (3) Balachari, D; Org Lett 2000, V2, P863 HCPLUS
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  - (8) Evans, D; Aldrichimica Acta 1982, V2, P23
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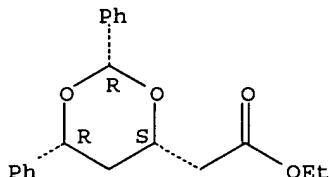
IT 337508-83-5P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (asym. synthesis of benzylidene-dihydroxy carboxylates via enantio- and  
 regioselective Sharpless dihydroxylation and palladium-catalyzed reduction)

RN 337508-83-5 HCPLUS

CN 1,3-Dioxane-4-acetic acid, 2,6-diphenyl-, ethyl ester, (2R,4S,6R)- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L46 ANSWER 3 OF 10 HCPLUS COPYRIGHT 2005 ACS on STN

AN 1995:183540 HCPLUS

DN 122:30928

ED Entered STN: 12 Nov 1994

TI Utilization of the [CpMo(CO)2(η<sub>3</sub>-2-CH<sub>2</sub>COC<sub>3</sub>H<sub>4</sub>)]- Enolate for  
 Stereoselective Synthesis of (1R\*,3S\*)-4-Pentene-1,3-diolsAU Liao, Ming-Fea; Lee, Gene-Hsiang; Peng, Shie-Ming; Liu, Rai-Shung  
 CS Department of Chemistry, National Tsing-Hua University, Taiwan, 30043,  
 TaiwanSO Organometallics (1994), 13(12), 4973-7  
 CODEN: ORGND7; ISSN: 0276-7333

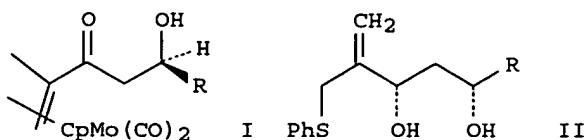
DT Journal

LA English

CC 23-7 (Aliphatic Compounds)

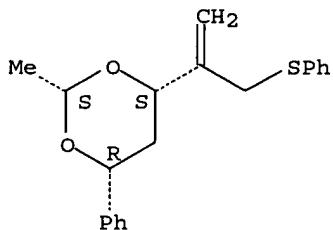
OS CASREACT 122:30928

GI



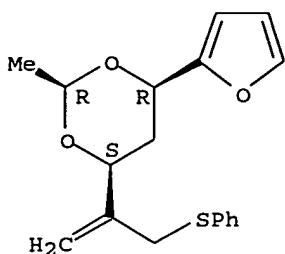
- AB** The enolate anion of  $[\text{CpMo}(\text{CO})_2(\eta^3\text{-2-CH}_3\text{COC}_3\text{H}_4)]$ , readily generated by lithium diisopropylamide in cold THF (-78 °C), underwent alkylation with aldehydes to give the aldol products I ( $\text{R} = \text{Ph}$ , 2-furyl, CMe<sub>3</sub>) in good yields. X-ray diffraction measurement of I ( $\text{R} = \text{Ph}$ ) shows strong intramol. hydrogen bonding within the ketone and alc. groups. The Me<sub>4</sub>NBH<sub>4</sub> reduction of I via proton-chelation control in benzene/CH<sub>3</sub>OH proceeded with fair diastereoselectivities in favor of the syn-1,3-diol. Addition of PhSNa to the NO<sup>+</sup> cation of the  $\pi$ -allyl syn-1,3-diols gave pentenediols II.
- ST** methylbutenone complex alkylation aldehyde; methylpentenediol complex; phenylthiomethylpentenediol; pentenediol phenylthiomethyl
- IT** Alkylation  
(preparation of pentenediols from methylbutenone molybdenum complex)
- IT** 159565-39-6P  
RL: BYP (Byproduct); PREP (Preparation)  
(preparation of pentenediols from methylbutenone molybdenum complex)
- IT** 98-01-1, Furfural, reactions 100-52-7, Benzaldehyde, reactions 630-19-3, Pivalaldehyde 4984-82-1, Cyclopentadienylsodium 150324-04-2  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of pentenediols from methylbutenone molybdenum complex)
- IT** 159558-11-9P 159558-12-0P 159558-13-1P 159565-31-8P 159565-32-9P  
159565-33-0P 159565-34-1P 159565-35-2P 159565-36-3P 159565-37-4P  
159565-38-5P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of pentenediols from methylbutenone molybdenum complex)
- IT** 159558-14-2P 159558-15-3P 159558-16-4P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of pentenediols from methylbutenone molybdenum complex)
- IT** 159558-14-2P 159558-15-3P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of pentenediols from methylbutenone molybdenum complex)
- RN** 159558-14-2 HCAPLUS
- CN** 1,3-Dioxane, 2-methyl-4-phenyl-6-[1-[(phenylthio)methyl]ethenyl]-, (2 $\alpha$ ,4 $\alpha$ ,6 $\alpha$ )- (9CI) (CA INDEX NAME)

Relative stereochemistry.



- RN** 159558-15-3 HCAPLUS
- CN** 1,3-Dioxane, 4-(2-furanyl)-2-methyl-6-[1-[(phenylthio)methyl]ethenyl]-, (2 $\alpha$ ,4 $\alpha$ ,6 $\alpha$ )- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L46 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1991:207415 HCAPLUS  
 DN 114:207415  
 ED Entered STN: 31 May 1991  
 TI Regio- and stereocontrolled functionalization of acyclic molybdenum- $\eta^3$ -allyl complexes  
 AU Vong, Wen Jung; Peng, Shie Ming; Lin, Shie Hsiung; Lin, Wen Jye; Liu, Rai Shung  
 CS Dep. Chem., Natl. Tsing Hua Univ., Hsinchu, 30043, Taiwan  
 SO Journal of the American Chemical Society (1991), 113(2), 573-82  
 CODEN: JACSAT; ISSN: 0002-7863  
 DT Journal  
 LA English  
 CC 29-11 (Organometallic and Organometalloidal Compounds)  
 Section cross-reference(s): 23, 75  
 OS CASREACT 114:207415  
 AB Chemical transformation of the ester  $CpMo(CO)_2(\text{syn}-\eta^3\text{-}1\text{-C}_3H_4COOMe)$  to its  $\eta^3$ -allyl alc., acid, acid chloride, and amide has been achieved. Treatment of  $CpMo(CO)_2(\text{syn}-\eta^3\text{-}1\text{-C}_3H_4CHROH)$  [R = H, CH<sub>3</sub> (I)] with (CF<sub>3</sub>SO<sub>2</sub>)<sub>2</sub>O in ether at -78° stereoselectively generates the air-stable s-trans- $\eta^4$ -diene cations, which have been characterized by appropriate phys. methods. The ionization process proceeds via an intramol. SN<sub>2</sub> mode. The s-trans- $\eta^4$ -cis-pentadiene cation reacts with water, alc., thiol, and amine to give  $\eta^3$ -allyl derivs., which retain the same configuration as that of I. The enolate  $CpMo(CO)_2(\text{syn}-\eta^3\text{-}1\text{-C}_3H_4COCH_2Li)$  condenses with aldehyde at -78° to yield the aldol products  $CpMo(CO)_2(\text{syn}-\eta^3\text{-}1\text{-C}_3H_4COCH_2CHROH)$  [R = Ph, CH<sub>3</sub> (II), (CH<sub>3</sub>)<sub>2</sub>CH] with good diastereoselectivity. The major diastereomer of II has been isolated and characterized by x-ray diffraction. Further reduction of this diastereomer with NaBH<sub>4</sub> produces the corresponding 1,3-diol as a single diastereomer. Utilization of I and  $CpMo(CO)_2[\text{syn}-\eta^3\text{-}1\text{-C}_3H_4CH(OH)CHPhOH}$  in synthesis of acyclic 1,3-diol and 1,3,5-triol has been achieved, with excellent stereoselectivity; a mechanism has been proposed.  
 ST molybdenum allyl regioselective stereoselective reaction; diol stereoselective prepn; triol stereoselective prepn; crystal mol structure cyclopentadienylmolybdenum allyl  
 IT Alcohols, preparation  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (dihydric and trihydric, stereoselective preparation of, from molybdenum allyl complexes)  
 IT Regiochemistry  
 Stereochemistry  
 (of reactions of molybdenum allyl complexes)  
 IT 100-52-7, Benzaldehyde, reactions  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (decomplexation by, of molybdenum allyl complex)  
 IT 131297-49-9P 131349-97-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and amidation of)  
 IT 131349-74-1P 131349-75-2P 131349-93-4P

IT 131297-48-8P 131349-96-7P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and conversion of, to acid)

IT 131297-52-4P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and conversion of, to acid chloride)

IT 131297-56-8P 131432-32-1P  
 RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and crystal structure of)

IT 131297-44-4P 131297-45-5P 131297-46-6P 131297-47-7P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and decarbonylation of)

IT 131432-33-2P 131432-34-3P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and decomplexation of, with benzaldehyde)

IT 131139-27-0P 131349-73-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and hydrolysis of)

IT 131297-55-7P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and reaction of, with lithium chloride)

IT 128923-52-4P 129029-46-5P 131349-77-4P 131349-98-9P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and reaction of, with triflic anhydride)

IT 129029-47-6P 131175-74-1P 131297-50-2P 131297-51-3P 131349-76-3P  
 131349-95-6P 131349-99-0P 131350-00-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and reactions of)

IT 131101-67-2P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and reactions of, with methanol or water)

IT 129029-45-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and reactions of, with nucleophiles)

IT 128923-59-1P 131297-53-5P 131349-86-5P 131349-88-7P 131349-89-8P  
 131349-90-1P 131349-91-2P 131349-92-3P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and reduction of)

IT 128923-57-9P 131139-28-1P 131139-32-7P 131175-75-2P 131349-78-5P  
 131349-79-6P 131349-80-9P 131349-81-0P 131349-82-1P 131349-83-2P  
 131349-84-3P 131349-85-4P 131349-94-5P 131350-01-1P 131350-02-2P  
 131350-03-3P 131350-05-5P 131350-06-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

IT 128923-51-3P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation, crystal structure, and reactions of)

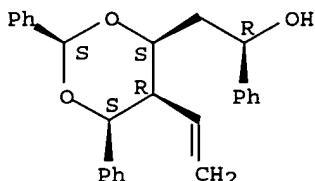
IT 131349-87-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation, crystal structure, and reduction of)

IT 12107-35-6  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with Me chlorobutenoate or with chloropentenone)

IT 15320-72-6 61170-81-8  
 RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction of, with cyclopentadienylmolybdenum anion)  
IT 131349-73-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and hydrolysis of)  
RN 131349-73-0 HCPLUS  
CN 1,3-Dioxane-4-ethanol, 5-ethenyl- $\alpha$ ,2,6-triphenyl-,  
[2 $\alpha$ ,4 $\alpha$ (S\*),5 $\alpha$ ,6 $\alpha$ ] - (9CI) (CA INDEX NAME)

Relative stereochemistry.



L46 ANSWER 5 OF 10 HCPLUS COPYRIGHT 2005 ACS on STN  
AN 1991:185675 HCPLUS  
DN 114:185675  
ED Entered STN: 17 May 1991  
TI Generation and aldol reaction of enolate anion adjacent to a  $\eta^3$ -allyl-Mo(CO)2Cp moiety. A new approach to the stereoselective synthesis of 1,3,5-triol and 2-vinyl-3-hydroxyl-tetrahydrofuran  
AU Lin, Shie Hsiung; Vong, Wen Jung; Cheng, Chih Yi; Wang, Sue Lein; Liu, Rai Shung  
CS Dep. Chem., Natl. Tsinghua Univ., Hsinchu, Taiwan  
SO Tetrahedron Letters (1990), 31(52), 7645-8  
CODEN: TELEAY; ISSN: 0040-4039  
DT Journal  
LA English  
CC 29-11 (Organometallic and Organometalloidal Compounds)  
Section cross-reference(s): 75  
AB The enolate of CpMo(CO)2(syn- $\eta^3$ -1-C3H4COCH3) generated with lithium diisopropylamide in THF undergoes diastereoselective aldol reaction with benzaldehyde; the alc. thus formed has been utilized for stereoselective synthesis of 1,5-diphenyl-2-vinyl-pentane-1,3,5-triol and 2-vinyl-3-hydroxy-5-phenyl-tetrahydrofuran.  
ST aldol reaction enolate allylmolybdenum benzaldehyde; triol vinylpentane; THF vinylhydroxyl; crystal structure allylmolybdenum hydroxymethyl ketone; mol structure allylmolybdenum hydroxymethyl ketone  
IT Crystal structure  
Molecular structure  
(of allylmolybdenum) hydroxymethyl ketone  
IT Aldol condensation  
(of allyl molybdenum enolate anion with benzaldehyde)  
IT 133090-82-1P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and chlorination of)  
IT 131175-72-9P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and deprotonation of, with lithium diisopropylamide)  
IT 131349-87-6P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and reduction of, with sodium borohydride)  
IT 129029-43-2P 131045-30-2P 131045-31-3P 131139-31-6P  
131139-32-7P 133068-00-5P 133345-41-2P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

IT 131349-90-1P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation, crystal and mol. structure and reduction of, with sodium borohydride)

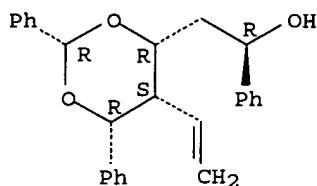
IT 12107-35-6  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with chloropentenone)

IT 61170-81-8  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with cyclopentadienolmangaonate complex)

IT 131139-31-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

RN 131139-31-6 HCPLUS  
 CN 1,3-Dioxane-4-ethanol, 5-ethenyl- $\alpha$ ,2,6-triphenyl-,  
 [2 $\alpha$ ,4 $\alpha$ (R\*),5 $\alpha$ ,6 $\alpha$ ] - (9CI) (CA INDEX NAME)

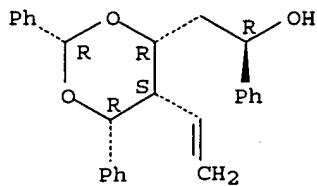
Relative stereochemistry.



L46 ANSWER 6 OF 10 HCPLUS COPYRIGHT 2005 ACS on STN  
 AN 1991:24103 HCPLUS  
 DN 114:24103  
 ED Entered STN: 26 Jan 1991  
 TI Stereocontrolled functionalization of acyclic molybdenum- $\eta$ 3-allyl complexes: a new approach to the stereoselective synthesis of 1,3-diols  
 AU Wong, Wen Jung; Lin, Shie Hsiung; Liu, Rai Shung; Lee, Gene Hsian; Peng, Shie Ming  
 CS Dep. Chem., Natl. Tsing Hua Univ., Hsinchu, 30043, Taiwan  
 SO Journal of the Chemical Society, Chemical Communications (1990),  
 (18), 1285-7  
 CODEN: JCCCAT; ISSN: 0022-4936  
 DT Journal  
 LA English  
 CC 29-11 (Organometallic and Organometalloidal Compounds)  
 Section cross-reference(s): 23, 75  
 OS CASREACT 114:24103  
 AB Functionalization of [CpMo(CO)2( $\eta$ 3-syn-1-C3H4COCH3)] (Cp =  $\eta$ 5-C5H5) proceeds in a highly stereospecific manner; the Mo- $\eta$ 3-allyl unit is effective in directing asym. carbon induction in the course of s-trans- $\eta$ 4-cis-pentadiene formation, aldol condensation and asym. 1,3-diol synthesis.  
 ST asym synthesis diol; aldol condensation stereoselective functionalized allylmolybdenum; pentadiene molybdenum asym induction; stereochem reaction functionalized allylmolybdenum; crystal structure functionalized allylmolybdenum  
 IT Asymmetric synthesis and induction  
 (of 1,3-diols from acyclic molybdenum allyl complexes)  
 IT Crystal structure  
 Molecular structure  
 (of functionalized allylmolybdenum complexes)  
 IT Stereochemistry  
 (of reactions of functionalized acyclic molybdenum allyl complexes)  
 IT Aldol condensation  
 (stereoselective, of functionalized allylmolybdenum complexes)  
 IT 131101-67-2P 131103-55-4P  
 RL: FORM (Formation, nonpreparative); PREP (Preparation)

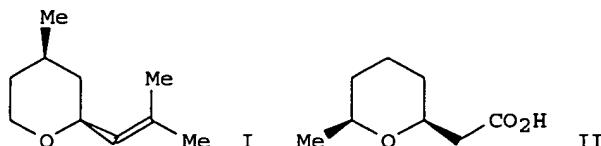
- (formation of, from isomerization of diene complex)
- IT 131045-31-3P 131082-91-2P 131082-92-3P 131082-93-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and reaction of, with benzaldehyde in presence of methanol,  
 stereochem. of)
- IT 128923-53-5P 131045-30-2P 131082-90-1P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and reaction of, with nitrosyl tetrafluoroborate and lithium chloride)
- IT 128923-52-4P 131082-89-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and reaction of, with triflic anhydride)
- IT 131139-31-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and stereoselective acid hydrolysis of)
- IT 131139-27-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and stereoselective hydrolysis of)
- IT 129029-45-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and stereoselective reactions of)
- IT 128923-64-8P 131139-28-1P 131139-29-2P 131139-30-5P 131139-32-7P  
 131175-74-1P 131175-75-2P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)
- IT 128923-60-4P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation, crystal structure, and stereoselective reduction of)
- IT 131175-72-9  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (stereoselective reduction and crystal structure of)
- IT 131082-88-7  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (stereoselective reduction of)
- IT 131139-31-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and stereoselective acid hydrolysis of)
- RN 131139-31-6 HCAPLUS
- CN 1,3-Dioxane-4-ethanol, 5-ethenyl- $\alpha$ ,2,6-triphenyl-,  
 [2 $\alpha$ ,4 $\alpha$ (R\*),5 $\alpha$ ,6 $\alpha$ ] - (9CI) (CA INDEX NAME)

Relative stereochemistry.



- L46 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1991:6220 HCAPLUS  
 DN 114:6220  
 ED Entered STN: 12 Jan 1991  
 TI Stereoselective syntheses of  $\alpha$ -substituted cyclic ethers and  
 syn-1,3-diols

AU Homma, Koichi; Takenoshita, Haruhiro; Mukaiyama, Teruaki  
 CS Org. Chem. Res. Lab., Tanabe Seiyaku Co., Ltd., Toda, 335, Japan  
 SO Bulletin of the Chemical Society of Japan (1990), 63(7), 1898-15  
 CODEN: BCSJA8; ISSN: 0009-2673  
 DT Journal  
 LA English  
 CC 27-13 (Heterocyclic Compounds (One Hetero Atom))  
 OS CASREACT 114:6220  
 GI



- AB** In the presence of a catalytic amount of triphenylmethylium hexachloroantimonate or a catalyst system of antimony pentachloride, chlorotrimethylsilane and tin(II) iodide,  $\alpha$ -substituted cyclic ethers are stereoselectively prepared from lactones by successive treatment with 1-(tert-butyldimethylsiloxy)-1-ethoxyethene and silyl nucleophiles such as triethylsilane, allyltrimethylsilane and trimethylsilyl cyanide. These catalysts also promote the reaction of  $\gamma$ -,  $\delta$ - and  $\epsilon$ -trimethylsiloxy carbonyl compds. with silyl nucleophiles resulting in the formation of  $\alpha$ -substituted cyclic ethers. The former procedure is effectively applied to short synthesis of (-)-cis-rose oxide (I), and (cis-6-methyltetrahydro-2-pyranyl)acetic acid (II), a constituent of civet. Furthermore, syn-1,3-diols are also stereoslectively prepared from lactone analog, 6-cis-substituted 2-(trichloromethyl)-1,3-dioxan-4-ones, easily prepared from  $\beta$ -hydroxycarboxylic acids.
- ST** ether cyclic alpha substituted; diol syn; lactone reaction silyloxyethoxyethene silyl nucleophile; carbonyl silyloxy reaction silyl nucleophile; rose oxide cis; methyltetrahydropyranylacetic acid
- IT** Lactones  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with (silyloxy)ethoxyethene, in presence of triphenylmethylium hexachloroantimonate)
- IT Carbonyl compounds, reactions  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (silyloxy, reaction of, with silyl nucleophiles, in presence of triphenylmethylium hexachloroantimonate)
- IT Ethers, preparation  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (cyclic, preparation of, from lactones and (silyloxy)ethoxyethenes)
- IT 10294-70-9, Stannous iodide  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (catalysts containing antimony pentachloride, chlorotrimethylsilane and, for reaction of lactones with (silyloxy)ethoxyethene)
- IT 75-77-4, Chlorotrimethylsilane, uses and miscellaneous  
 RL: USES (Uses)  
 (catalysts containing antimony pentachloride, tin iodide and, for reaction of lactones with (silyloxy)ethoxyethene)
- IT 7646-78-8, Stannic chloride, uses and miscellaneous 7647-18-9, Antimony pentachloride  
 RL: USES (Uses)  
 (catalysts containing chlorotrimethylsilane, tin iodide and, for reaction of lactones with (silyloxy)ethoxyethene)
- IT 437-18-3, Triphenylmethyl hexafluoroantimonate 1586-91-0,  
 Triphenylmethyl hexachloroantimonate 3058-33-1  
 RL: CAT (Catalyst use); USES (Uses)  
 (catalysts, for reaction of lactones with (silyloxy)ethoxyethene)

IT 300-85-6 3480-87-3 23985-59-3 130822-12-7 130822-13-8  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (cyclocondensation of, with chloral)

IT 75-87-6, Chloral  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (cyclocondensation of, with hydroxypropionic acids)

IT 79936-64-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and Grignard reaction of, with methylmagnesium bromide)

IT 130822-03-6P 130822-27-4P  
 RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and crystal structure of)

IT 130822-24-1P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and cyclization of)

IT 79981-82-1P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and dehydration of)

IT 124468-82-2P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and hydrolysis of)

IT 127801-68-7P 127801-69-8P 127801-70-1P 127801-71-2P 127822-99-5P  
 127910-15-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and reaction of, with (silyloxy)ethoxyethene)

IT 130822-02-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and reaction of, with naphthyl isocyanate)

IT 127801-72-3P 127801-73-4P 127801-74-5P 127801-75-6P  
 127801-76-7P 127910-16-1P 127910-17-2P 128316-90-5P  
 128316-91-6P 128316-92-7P 128316-93-8P 128316-94-9P  
 130822-00-3P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and reduction of)

IT 130822-19-4P 130822-20-7P 130822-21-8P 130822-22-9P  
 130822-23-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and ring cleavage of)

IT 2434-02-8P 3033-23-6P, (-)-cis-Rose oxide 4203-44-5P 16133-83-8P  
 38786-78-6P 76985-22-3P 87172-73-4P 107400-64-6P 119873-45-9P  
 119873-46-0P 119873-47-1P 119873-48-2P 119873-49-3P 119873-50-6P  
 121029-82-1P 124468-71-9P 124468-72-0P 124468-74-2P 124468-75-3P  
 124468-76-4P 124468-77-5P 124468-78-6P 124468-81-1P 124468-83-3P  
 124469-04-1P 124469-05-2P 124469-06-3P 124469-07-4P 124469-09-6P  
 124578-87-6P 127910-18-3P 130821-85-1P 130822-01-4P 130822-04-7P  
 130822-26-3P 130822-28-5P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

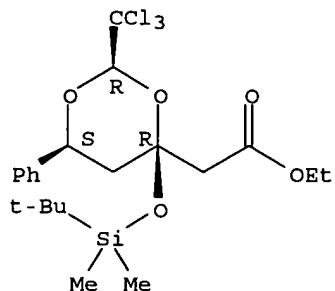
IT 61898-55-3  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with (silyloxy)ethoxyethene)

IT 96-48-0,  $\gamma$ -Butyrolactone 108-29-2 502-44-3, 2-Oxepanone  
 542-28-9,  $\delta$ -Valerolactone 823-22-3 1121-84-2 1679-47-6  
 2549-59-9 2549-61-3 3123-98-6 10603-03-9  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with (silyloxy)ethoxyethene and silyl nucleophile)

IT 42201-84-3  
 RL: RCT (Reactant); RACT (Reactant or reagent)

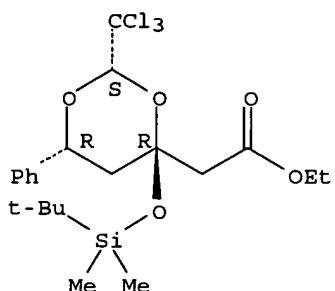
(reaction of, with lactones, catalysts for)  
IT 124468-98-0 124468-99-1 124469-00-7 124469-01-8 124469-02-9  
124469-03-0  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with silyl nucleophile)  
IT 127801-73-4P 127910-17-2P 128316-91-6P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and reduction of)  
RN 127801-73-4 HCPLUS  
CN 1,3-Dioxane-4-acetic acid, 4-[[((1,1-dimethylethyl)dimethylsilyl)oxy]-6-  
phenyl-2-(trichloromethyl)-, ethyl ester, (2 $\alpha$ ,4 $\alpha$ ,6 $\alpha$ )-  
(9CI) (CA INDEX NAME)

Relative stereochemistry.



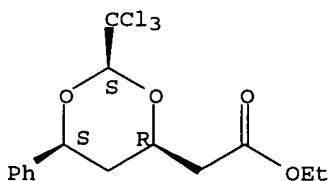
RN 127910-17-2 HCPLUS  
CN 1,3-Dioxane-4-acetic acid, 4-[[((1,1-dimethylethyl)dimethylsilyl)oxy]-6-  
phenyl-2-(trichloromethyl)-, ethyl ester, (2 $\alpha$ ,4 $\beta$ ,6 $\alpha$ )-  
(9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 128316-91-6 HCPLUS  
CN 1,3-Dioxane-4-acetic acid, 6-phenyl-2-(trichloromethyl)-, ethyl ester,  
(2 $\alpha$ ,4 $\alpha$ ,6 $\alpha$ )- (9CI) (CA INDEX NAME)

Relative stereochemistry.

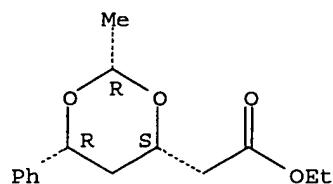


IT 130822-20-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

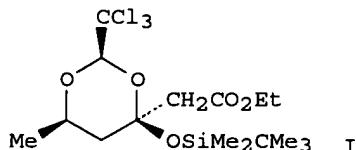
(Reactant or reagent)  
(preparation and ring cleavage of)

RN 130822-20-7 HCAPLUS  
CN 1,3-Dioxane-4-acetic acid, 2-methyl-6-phenyl-, ethyl ester,  
(2 $\alpha$ ,4 $\alpha$ ,6 $\alpha$ ) - (9CI) (CA INDEX NAME)

Relative stereochemistry.



L46 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN  
AN 1990:459054 HCAPLUS  
DN 113:59054  
ED Entered STN: 17 Aug 1990  
TI Stereoselective reduction of tert-butyldimethylsiloxy group of ethyl  
2-(trichloromethyl)-4-(tert-butyldimethylsiloxy)-1,3-dioxan-4-acetates  
AU Homma, Koichi; Mukaiyama, Teruaki  
CS Fac. Sci., Univ. Tokyo, Tokyo, 162, Japan  
SO Heterocycles (1990), 31(3), 443-6  
CODEN: HTCYAM; ISSN: 0385-5414  
DT Journal  
LA English  
CC 28-11 (Heterocyclic Compounds (More Than One Hetero Atom))  
OS CASREACT 113:59054  
GI



AB The tert-Butyldimethylsiloxy group of Et 4-tert-butyldimethylsiloxy-2-trichloromethyl-1,3-dioxan-4-acetates (I) was stereoselectively reduced with triethylsilane to Et cis-2-trichloromethyl-1,3-dioxan-4-acetates by using titanium tetrachloride as a promoter.  
ST stereoselective redn butyldimethylsiloxytrichloromethyldioxanacetate  
titanium tetrachloride  
IT Lewis acids  
RL: CAT (Catalyst use); USES (Uses)  
(catalyst, for stereoselective reduction of tert-butyldimethylsiloxy group)  
IT Reduction  
(stereoselective, of tert-butyldimethylsiloxy group in Et  
(trichloromethyl)(tert-butyldimethylsiloxy)dioxanacetates with titanium  
tetrachloride)  
IT Reduction catalysts  
(stereoselective, titanium tetrachloride, for tert-butyldimethylsiloxy  
group in Et (trichloromethyl)(tert-butyldimethylsiloxy)dioxanacetates)  
IT 7446-70-0, Aluminum trichloride, uses and miscellaneous 7550-45-0,  
Titanium chloride (TiCl4) (T-4)-, uses and miscellaneous 7646-78-8, Tin  
tetrachloride, uses and miscellaneous  
RL: CAT (Catalyst use); USES (Uses)  
(catalyst, for stereoselective reduction of tert-butyldimethylsiloxy group  
of Et (trichloromethyl)(tert-butyldimethylsiloxy)dioxanacetates)

IT 128316-90-5P 128316-91-6P 128316-92-7P 128316-93-8P  
 128316-94-9P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

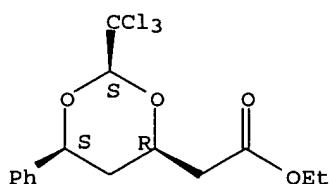
IT 127801-72-3 127801-73-4 127801-74-5 127801-75-6  
 127801-76-7 127910-16-1 127910-17-2  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (stereoselective reduction of, with triethylsilane in presence of titanium tetrachloride)

IT 128316-91-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

RN 128316-91-6 HCAPLUS

CN 1,3-Dioxane-4-acetic acid, 6-phenyl-2-(trichloromethyl)-, ethyl ester,  
 $(2\alpha, 4\alpha, 6\alpha)$  - (9CI) (CA INDEX NAME)

Relative stereochemistry.

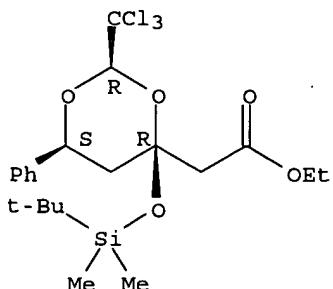


IT 127801-73-4 127910-17-2  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (stereoselective reduction of, with triethylsilane in presence of titanium tetrachloride)

RN 127801-73-4 HCAPLUS

CN 1,3-Dioxane-4-acetic acid, 4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-phenyl-2-(trichloromethyl)-, ethyl ester,  $(2\alpha, 4\alpha, 6\alpha)$  - (9CI) (CA INDEX NAME)

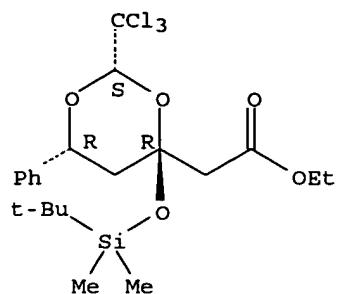
Relative stereochemistry.



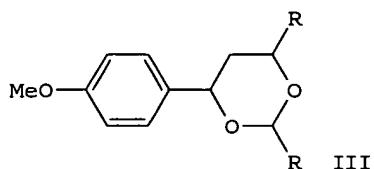
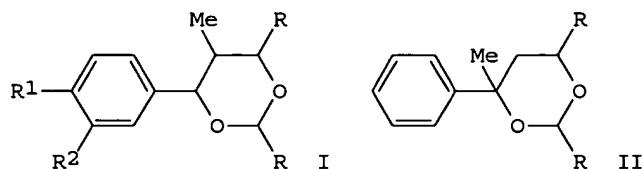
RN 127910-17-2 HCAPLUS

CN 1,3-Dioxane-4-acetic acid, 4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-phenyl-2-(trichloromethyl)-, ethyl ester,  $(2\alpha, 4\beta, 6\alpha)$  - (9CI) (CA INDEX NAME)

Relative stereochemistry.



L46 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1986:591018 HCAPLUS  
 DN 105:191018  
 ED Entered STN: 28 Nov 1986  
 TI Condensation of aromatic alkenes with aldehydes catalyzed by ion-exchange resins. III. Aliphatic aldehydes  
 AU El Gharbi, R.; Delmas, M.; Gaset, A.  
 CS Lab. Synth. Phys.-Chim. Org., Ec. Natl. Ing. Sfax, Sfax, 3038, Tunisia  
 SO Tetrahedron (1986), 42(4), 1191-8  
 CODEN: TETRAB; ISSN: 0040-4020  
 DT Journal  
 LA French  
 CC 28-11 (Heterocyclic Compounds (More Than One Hetero Atom))  
 OS CASREACT 105:191018  
 GI



AB Condensation of 4,3-R1R2C6H3CH:CHMe (R1 = MeO, OH; R2 = H, MeO; R1R2 = OCH2O) or PhCMe:CH2 with aliphatic aldehydes RCHO (R = Et, Pr, Bu, n-C5H11) gave isomers of dioxanes I and II, resp. The reaction was catalyzed by ionic exchange resins. On the other hand, condensation of RCHO (same R) with 4-MeOC6H4CH:CH2 gave single isomers of the 1,3-dioxanes III.  
 ST condensation alkanal alkene phenyl; aldehyde aliph condensation phenyl alkene; dioxane; dioxacyclohexane  
 IT Condensation reaction catalysts  
 (ion exchange resins, for phenyl-substituted alkenes with aldehydes)  
 IT Cyclocondensation reaction catalysts  
 (ion exchange resins, for phenyl-substituted alkenes with aliphatic aldehydes)  
 IT Condensation reaction  
 Cyclocondensation reaction  
 (of phenyl-substituted alkenes with aliphatic aldehydes)  
 IT Alkenes, reactions  
 RL: RCT (Reactant); RACT (Reactant or reagent)

(phenyl-substituted, condensation with aliphatic aldehydes)

IT Aldehydes, reactions  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (aliphatic, condensation with phenyl-substituted alkenes)

IT 97-54-1 98-83-9, reactions 104-46-1 120-58-1 637-69-4  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (condensation of, with aliphatic aldehydes)

IT 66-25-1 110-62-3 123-38-6, reactions 123-72-8  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (condensation of, with phenyl-substituted alkenes)

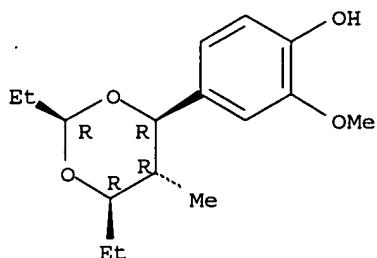
IT 78703-13-6P 78703-14-7P 78703-15-8P 78703-16-9P 78779-40-5P  
 78779-41-6P 104789-86-8P 104789-87-9P 104789-88-0P 104789-89-1P  
 104789-90-4P 104789-91-5P 104789-92-6P 104789-93-7P  
 104789-94-8P 104789-95-9P 104789-96-0P 104789-97-1P  
 104789-98-2P 104789-99-3P 104790-00-3P 104790-01-4P 104871-48-9P  
 104871-49-0P 104871-50-3P 104871-51-4P 104871-52-5P 104871-53-6P  
 104871-54-7P 104871-55-8P 104871-56-9P 104871-57-0P 104871-58-1P  
 104871-59-2P 104871-60-5P 104871-61-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

IT 104789-94-8P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

RN 104789-94-8 HCAPLUS

CN Phenol, 4-(2,6-diethyl-5-methyl-1,3-dioxan-4-yl)-2-methoxy-,  
 (2 $\alpha$ ,4 $\alpha$ ,5 $\beta$ ,6 $\alpha$ ) - (9CI) (CA INDEX NAME)

Relative stereochemistry.



L46 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1967:115660 HCAPLUS  
 DN 66:115660  
 ED Entered STN: 12 May 1984  
 TI Condensation reactions of  $\alpha,\alpha$ -dimorpholinoacetic acid and glyoxylic acid on olefins  
 AU Kurfanto, Michel; Le Roy, Pierre; Vene, Jean  
 CS Ecole Natl. Super. Chim. Rennes, Rennes, Fr.  
 SO Comptes Rendus des Seances de l'Academie des Sciences, Serie C: Sciences  
 Chimiques (1967), 264(2), 232-5  
 CODEN: CHDCAQ; ISSN: 0567-6541  
 DT Journal  
 LA French  
 CC 28 (Heterocyclic Compounds (More Than One Hetero Atom))  
 OS CASREACT 66:115660  
 GI For diagram(s), see printed CA Issue.  
 AB  $\alpha,\alpha$ -Dimorpholinoacetic acid (I), prepared from  $\alpha,\alpha$ -dichloroacetic acid and morpholine, reacts with an olefin in concentrated H<sub>2</sub>SO<sub>4</sub> to give II. A solid mixture of the morpholinium salt of I and morpholinium chloride is dispersed in an HOAc-H<sub>2</sub>SO<sub>4</sub> mixture, the olefin is added, and the mixture heated with rapid agitation for 10-40 hrs. at 50-60°. The following II are obtained (R1, R2, R3, % yield, and m.p. given): H, 4-MeOC<sub>6</sub>H<sub>4</sub>, H, 68, 150°; H, 4-MeC<sub>6</sub>H<sub>4</sub>, H, 40, 113°; H, 3-MeC<sub>6</sub>H<sub>4</sub>, H, 42, 96°; H, Ph, H, 43-5, 77°;

H, 4-BrC<sub>6</sub>H<sub>4</sub>, H, 30, 126°; H, 4-ClC<sub>6</sub>H<sub>4</sub>, H, 30, 127°; H, 3-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>, H, 10-15, 128°; Me, Ph, H, 73, - (b0.4 180°); H, 3,4-(MeO)(HO)C<sub>6</sub>H<sub>3</sub>, Me, 60, 183°; H, 4-MeOC<sub>6</sub>H<sub>4</sub>, Me, 70, 169°.

In the presence of H<sub>2</sub>O, results are obtained similar to those in the reaction of HO<sub>2</sub>CCHO (III) on olefins. The presence of HOAc and H<sub>2</sub>O leads to the formation of variable proportions of  $\alpha$ -acetoxybutyrolactone (IV, R = OAc). The condensation of olefins with com. 40% or 80% III gives principally IV (R = OH). When R<sub>1</sub> = R<sub>3</sub> = H, the  $\gamma$ -oxo acid, R<sub>2</sub>CO(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>H (V), isomeric with the hydroxylactone, is also formed. With p-Cl- and p-BrC<sub>6</sub>H<sub>4</sub>CH:CH<sub>2</sub>, a 2,4-dicarboxy-1,3-dioxane, (VI) was isolated and identified by ir and N.M.R. spectra. The following IV (R = OH) are prepared (R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, % yield with 40% III, % yield with 80% III, and m.p. given): H, Ph, H, 60, 62, 125°; H, 4-MeC<sub>6</sub>H<sub>4</sub>, H, 35, 45, 81°; H, 3-MeC<sub>6</sub>H<sub>4</sub>, H, 36, 45, 66°; H, 4-ClC<sub>6</sub>H<sub>4</sub>, H, 20, 55, 125°; H, 4-BrC<sub>6</sub>H<sub>4</sub>, H, -, 60, 132°; H, 3-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>, H, -, 20, 112°; Me, Ph, H, 65, 62, 97°; H, 3,4-(MeO)(HO)C<sub>6</sub>H<sub>3</sub>, Me, 60, 70, 155°; H, 4-MeOC<sub>6</sub>H<sub>4</sub>, Me, 50, 48, 110°. IV (R = OAc) and V prepared are (R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, m.p. or b.p. of IV, and m.p. of V given): H, Ph, H, m. 89°, 116°; H, 4-MeC<sub>6</sub>H<sub>4</sub>, H, b0.4 162°, 127°; H, 3-MeC<sub>6</sub>H<sub>4</sub>, H, b0.4 170°, 115°; H, 4-ClC<sub>6</sub>H<sub>4</sub>, H, m. 94°, 133°; H, 4-BrC<sub>6</sub>H<sub>4</sub>, H, m. 98°, 148°; H, 3-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>, H, m. 89°, 165°; Me, Ph, H, b0.3 152°, -; H, 3,4-(MeO)(AcO)C<sub>6</sub>H<sub>3</sub>, Me, m. 145°, -; H, 4-MeOC<sub>6</sub>H<sub>4</sub>, Me, m. 69°, -. Also prepared are VI (R = 4-ClC<sub>6</sub>H<sub>4</sub>), m. 213°, then 238° (di-Me ester m. 56°); and VI (R = 4-BrC<sub>6</sub>H<sub>4</sub>), m. 218°, then 239°; di-Me ester m. 88°.

IT Olefins, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)  
(with dimorpholinoacetic acid and glyoxylic acid)

IT Acetic acid, dimorpholino-

RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction with olefins)

IT 13397-35-8P 13983-50-1P 13983-51-2P 13983-52-3P 13983-53-4P  
13983-54-5P 13983-55-6P 13983-56-7P 13983-57-8P 13983-58-9P  
13983-59-0P 13983-60-3P 13983-61-4P 13983-62-5P 13983-63-6P  
13983-64-7P 13983-65-8P 13983-67-0P 13983-68-1P 13983-69-2P  
13983-70-5P 13983-71-6P 13983-72-7P 13983-73-8P 13983-74-9P  
13983-75-0P 13983-76-1P 13983-77-2P 13983-78-3P 13984-80-0P  
13984-81-1P 14060-45-8P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

IT 298-12-4

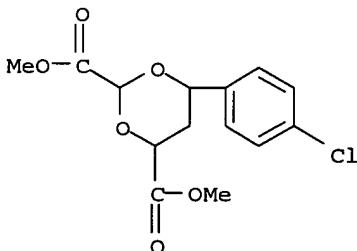
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction with olefins)

IT 13984-80-0P 13984-81-1P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RN 13984-80-0 HCPLUS

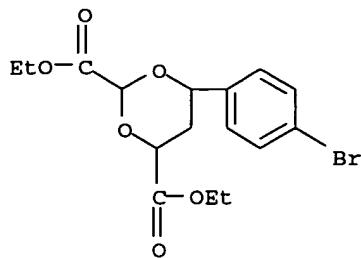
CN m-Dioxane-2,4-dicarboxylic acid, 6-(p-chlorophenyl)-, dimethyl ester (8CI)  
(CA INDEX NAME)



RN 13984-81-1 HCPLUS

CN m-Dioxane-2,4-dicarboxylic acid, 6-(p-bromophenyl)-, diethyl ester (8CI)

(CA INDEX NAME)



=> b uspatall  
FILE 'USPATFULL' ENTERED AT 12:01:04 ON 16 NOV 2005  
CA INDEXING COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 12:01:04 ON 16 NOV 2005  
CA INDEXING COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

=> d bib abs fhitstr hitrn l47 tot

L47 ANSWER 1 OF 4 USPATFULL on STN  
AN 2005:144167 USPATFULL  
TI Human papillomavirus inhibitors  
IN Meneses, Patricio I., Philadelphia, PA, UNITED STATES  
Koehler, Angela N., Cambridge, MA, UNITED STATES  
Wong, Jason C., Oberlin, OH, UNITED STATES  
Howley, Peter M., Wellesley, MA, UNITED STATES  
Schreiber, Stuart L., Boston, MA, UNITED STATES  
PA President and Fellows of Harvard College (U.S. corporation)  
PI US 2005123902 A1 20050609  
AI US 2004-851407 A1 20040521 (10)  
PRAI US 2003-472261P 20030521 (60)  
DT Utility  
FS APPLICATION  
LREP CHOCATE, HALL & STEWART LLP, EXCHANGE PLACE, 53 STATE STREET, BOSTON, MA,  
02109, US  
CLMN Number of Claims: 65  
ECL Exemplary Claim: 1  
DRWN 3 Drawing Page(s)  
LN.CNT 1845

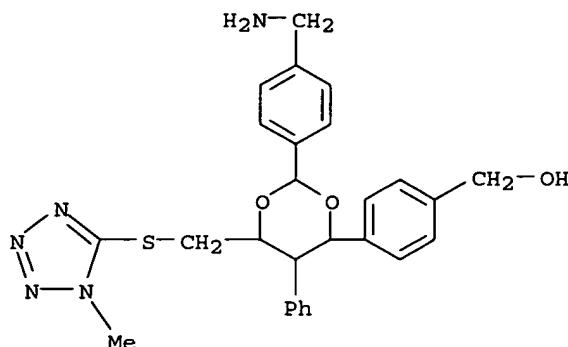
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides systems for identifying anti-viral agents. In particular, the invention encompasses reagents and strategies for identifying agents that inhibit or disrupt key protein-protein interactions that are important in the life cycle of papillomaviruses. The invention allows identification, production, and/or use of agents that reduce or inhibit the replication of HPV by inhibiting (e.g., precluding, reversing, or disrupting) the formation of the E1-E2 protein-protein complex. The invention also provides specific inhibitory agents, pharmaceutical compositions, and methods of using these inhibitors and pharmaceutical compositions for inhibiting viral replication in vitro. Methods are also described for the treatment and prevention of HPV infections and HPV-related diseases in patients.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 852992-28-0  
(as antiviral agent inhibiting papillomavirus replication; human  
papillomavirus inhibitors and screening system reagents)  
RN 852992-28-0 USPATFULL  
CN Benzenemethanol, 4-[2-[4-(aminomethyl)phenyl]-6-[[1-methyl-1H-tetrazol-5-

yl)thio]methyl]-5-phenyl-1,3-dioxan-4-yl]- (9CI) (CA INDEX NAME)



- IT 852992-28-0  
     (as antiviral agent inhibiting papillomavirus replication; human papillomavirus inhibitors and screening system reagents)
- IT 852992-29-1P 852992-30-4P  
     (as antiviral agent inhibiting papillomavirus replication; human papillomavirus inhibitors and screening system reagents)
- IT 852992-29-1DP, resin-bound  
     (human papillomavirus inhibitors and screening system reagents)

L47 ANSWER 2 OF 4 USPATFULL on STN

AN 2004:95394 USPATFULL

TI Dioxanes and uses thereof

IN Schreiber, Stuart L., Boston, MA, UNITED STATES  
           Sternson, Scott M., New York, NY, UNITED STATES  
           Wong, Jason C., Cambridge, MA, UNITED STATES  
           Grozinger, Christina M., Urbana, IL, UNITED STATES  
           Haggarty, Stephen J., Somerville, MA, UNITED STATES  
           Koeller, Kathryn M., Seattle, WA, UNITED STATES

PI US 2004072849 A1 20040415

AI US 2003-621276 A1 20030717 (10)

RLI Continuation-in-part of Ser. No. US 2002-144316, filed on 9 May 2002,  
     PENDING

PRAI US 2001-289850P 20010509 (60)

DT Utility

FS APPLICATION

LREP PATENT DEPARTMENT, CHOATE, HALL & STEWART, Exchange Place, 53 State Street, Boston, MA, 02109

CLMN Number of Claims: 65

ECL Exemplary Claim: 1

DRWN 78 Drawing Page(s)

LN.CNT 7435

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB In recognition of the need to develop novel therapeutic agents and efficient methods for the synthesis thereof, the present invention provides novel compounds of general formula (I): ##STR1##

and pharmaceutically acceptable derivatives thereof, wherein R.<sup>1</sup>, R.<sup>2</sup>, R.<sup>3</sup>, n, X and Y are as defined herein. The present invention also provides pharmaceutical compositions comprising a compound of formula (I) and a pharmaceutically acceptable carrier. The present invention further provides compounds capable of inhibiting histone deacetylase activity and methods for treating disorders regulated by histone deacetylase activity (e.g., cancer and protozoal infections) comprising administering a therapeutically effective amount of a compound of formula (I) to a subject in need thereof. The present invention additionally provides methods for modulating the glucose-sensitive subset of genes downstream of Ure2p. The present

invention also provides methods for preparing compounds of the invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

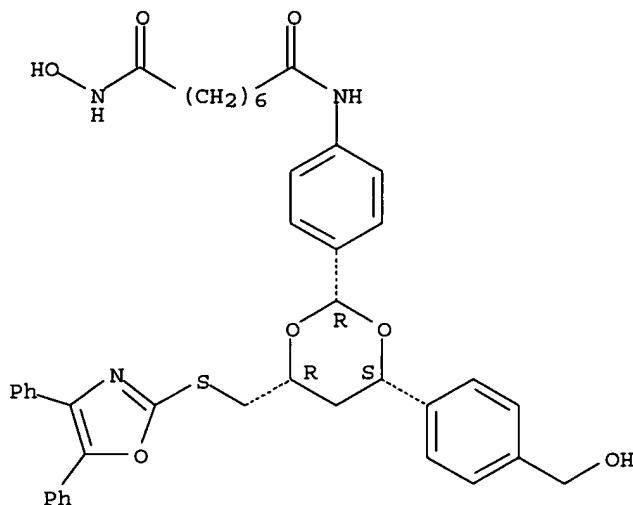
IT 537049-40-4P, Tubacin

(claimed compound; preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

RN 537049-40-4 USPATFULL

CN Octanediamide, N-[4-[(2R,4R,6S)-4-[[[(4,5-diphenyl-2-oxazolyl)thio]methyl]-6-[4-(hydroxymethyl)phenyl]-1,3-dioxan-2-yl]phenyl]-N'-hydroxy-, rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 537049-40-4P, Tubacin

(claimed compound; preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

IT 332925-20-9P 394657-68-2P 394657-69-3P

475161-04-7P

(preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

L47 ANSWER 3 OF 4 USPATFULL on STN

AN 2003:266010 USPATFULL

TI Dioxanes and uses thereof

IN Schreiber, Stuart L., Boston, MA, UNITED STATES

Sternson, Scott M., New York, NY, UNITED STATES

Wong, Jason C., Cambridge, MA, UNITED STATES

Grozinger, Christina M., Champagne, IL, UNITED STATES

PI US 2003187027 A1 20031002

AI US 2002-144316 A1 20020509 (10)

PRAI US 2001-289850P 20010509 (60)

DT Utility

FS APPLICATION

LREP Choate, Hall & Stewart, Exchange Place, 53 State Street, Boston, MA, 02109

CLMN Number of Claims: 38

ECL Exemplary Claim: 1

DRWN 26 Drawing Page(s)

LN.CNT 3455

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

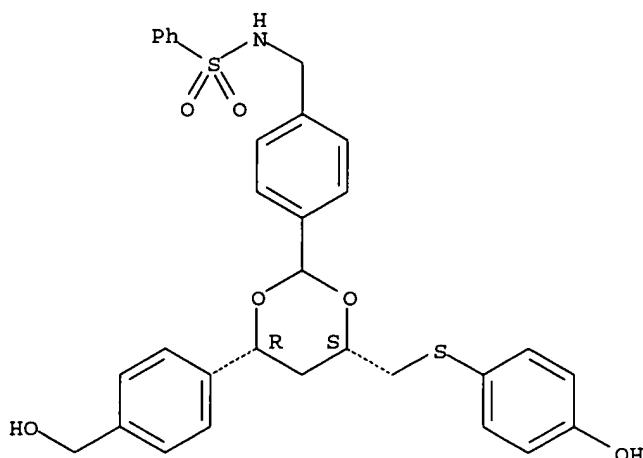
AB In recognition of the need to develop novel therapeutic agents and efficient methods for the synthesis thereof, the present invention provides novel compounds of general formula (I): ##STR1##

and pharmaceutically acceptable derivatives thereof, wherein R.sup.1, R.sup.2, R.sup.3, n, X and Y are as defined herein. The present invention also provides pharmaceutical compositions comprising a compound of formula (I) and a pharmaceutically acceptable carrier. The present invention further provides compounds capable of inhibiting histone deacetylase activity and methods for treating disorders regulated by histone deacetylase activity (e.g., cancer and protozoal infections) comprising administering a therapeutically effective amount of a compound of formula (I) to a subject in need thereof. The present invention additionally provides methods for modulating the glucose-sensitive subset of genes downstream of Ure2p.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 332925-20-9P  
 (preparation of dioxanes as inhibitors of histone deacetylase)  
 RN 332925-20-9 USPATFULL  
 CN Benzenesulfonamide, N-[4-[(4R,6S)-4-[4-(hydroxymethyl)phenyl]-6-[(4-hydroxyphenyl)thio]methyl]-1,3-dioxan-2-yl]phenyl]methyl], rel- (9CI)  
 (CA INDEX NAME)

Relative stereochemistry.



IT 332925-20-9P 394657-68-2P 475161-03-6P  
 475161-04-7P 475161-06-9P  
 (preparation of dioxanes as inhibitors of histone deacetylase)

L47 ANSWER 4 OF 4 USPATFULL on STN  
 AN 2003:120349 USPATFULL  
 TI Synthesis of combinatorial libraries of compounds reminiscent of natural products  
 IN Schreiber, Stuart L., Boston, MA, UNITED STATES  
 Shair, Matthew D., Somerville, MA, UNITED STATES  
 Tan, Derek S., Rochester, NY, UNITED STATES  
 Foley, Michael A., Somerville, MA, UNITED STATES  
 Stockwell, Brent R., Boston, MA, UNITED STATES  
 PI US 2003082830 A1 20030501  
 AI US 2002-185364 A1 20020627 (10)  
 RLI Continuation of Ser. No. US 1998-121922, filed on 25 Jul 1998, GRANTED,  
 Pat. No. US 6448443 Continuation-in-part of Ser. No. US 1997-951930,  
 filed on 16 Oct 1997, PENDING  
 PRAI US 1996-29128P 19961016 (60)  
 US 1997-49864P 19970606 (60)  
 DT Utility  
 FS APPLICATION  
 LREP Choate, Hall & Stewart, Exchange Place, 53 State Street, Boston, MA,  
 02109

CLMN Number of Claims: 6  
 ECL Exemplary Claim: 1  
 DRWN 50 Drawing Page(s)  
 LN.CNT 1716

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides complex compounds reminiscent of natural products and libraries thereof, as well as methods for their production. The inventive compounds and libraries of compounds are reminiscent of natural products in that they contain one or more stereocenters, and a high density and diversity of functionality. In general, the inventive libraries are synthesized from diversifiable scaffold structures, which are synthesized from readily available or easily synthesizable template structures. In certain embodiments, the inventive compounds and libraries are generated from diversifiable scaffolds synthesized from a shikimic acid based epoxyol template. In other embodiments, the inventive compounds and libraries are generated from diversifiable scaffolds synthesized from the pyridine-based template isonicotinamide. The present invention also provides a novel ortho-nitrobenzyl photolinker and a method for its synthesis. Furthermore, the present invention provides methods and kits for determining one or more biological activities of members of the inventive libraries. Additionally, the present invention provides pharmaceutical compositions containing one or more library members.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

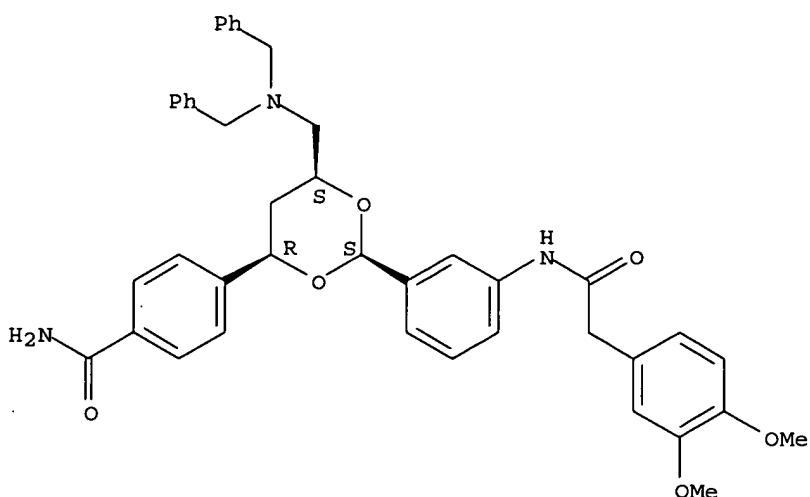
IT 206537-12-4P

(droplet assay system for simultaneously assaying combinatorial libraries and identifying compds. of chemical or biol. activities)

RN 206537-12-4 USPATFULL

CN Benzeneacetamide, N-[3-[(2S,4R,6S)-4-[4-(aminocarbonyl)phenyl]-6-[[bis(phenylmethyl)amino]methyl]-1,3-dioxan-2-yl]phenyl]-3,4-dimethoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 206537-12-4P

(droplet assay system for simultaneously assaying combinatorial libraries and identifying compds. of chemical or biol. activities)

=> d his

(FILE 'HOME' ENTERED AT 11:17:47 ON 16 NOV 2005)

FILE 'HCAPLUS' ENTERED AT 11:18:17 ON 16 NOV 2005

L1            2 (US2004072849 OR US2003187027) /PN OR (US2003-621276# OR US2002-  
       E SCHREIBER S/AU  
L2            119 E3,E5  
       E SCHREIBER STUART/AU  
L3            423 E3-6  
       E STERNSON S/AU  
L4            10 E4-5  
       E GROZINGER C/AU  
L5            16 E3-6  
       E HOGGARTY S/AU  
       E KOELLER K/AU  
L6            24 E5,E7-8  
L7            84766 HARVARD/CS, PA  
       E HOWARD HUGHES/CS, PA  
L8            16075 (HOWARD (1W) (HUGHES OR HUGHEES))/CS, PA

FILE 'REGISTRY' ENTERED AT 11:24:07 ON 16 NOV 2005

FILE 'HCAPLUS' ENTERED AT 11:24:07 ON 16 NOV 2005

L9            TRA L1 1- RN :            66 TERMS

FILE 'REGISTRY' ENTERED AT 11:24:08 ON 16 NOV 2005

L10            66 SEA L9  
L11            20 10 AND OCOC3/ES AND 46.150.18/RID AND NCOC2/ES  
L12            1 L11 AND 6/NR  
L13            14 C37H41N3O7S  
L14            0 L13 AND L11  
L15            0 L13 AND OCOC3/ES  
L16            STR  
L17            3 L16  
L18            567 L16 FULL  
       SAV TEM L18 WARD276F0/A  
L19            STR L16  
L20            4 L19 SAM SUB=L18  
L21            82 L19 FULL SUB=L18  
       SAV TEM WARD276S0/A L21  
L22            10 L21 AND NCOC2/ES  
L23            1 C41H43N3O7S AND L22  
L24            6 C41H43N3O7S  
L25            5 L24 NOT L23  
L26            STR L16  
L27            9 L26 SAM SUB=L18  
       SAV TEM L27 WARD276S1/A  
L28            88 L21,L27  
L29            7 L28 AND L10  
L30            79 L28 NOT CCS/CI  
       E A/CI  
L31            9 L28 NOT L30

FILE 'HCAPLUS' ENTERED AT 11:45:41 ON 16 NOV 2005

FILE 'HCAOLD' ENTERED AT 11:45:46 ON 16 NOV 2005

L32            0 L30

FILE 'HCAPLUS' ENTERED AT 11:45:56 ON 16 NOV 2005

L33            61 L30  
L34            13 L33 AND L1-8  
L35            48 L33 NOT L34  
L36            8 L23  
L37            6 L36 AND L1-8  
L38            13 L34,L37  
L39            2 L36 NOT L37  
L40            48 L35,L39  
L41            QUE PY<=2001 OR AY<=2001 OR PRY<=2001 OR PD<=20010509 OR AD<200  
L42            35 L40 AND L41

L43           0 L39 AND L41  
          SEL HIT RN L42

L44       FILE 'REGISTRY' ENTERED AT 11:51:33 ON 16 NOV 2005  
        49 E1-49  
          SEL RN 5 11 29 30 34-37 44 48 49 L44

L45       11 E50-60 AND L44

L46       FILE 'HCAPLUS' ENTERED AT 11:57:25 ON 16 NOV 2005  
        10 L45 AND L42

L47       FILE 'USPATFULL, USPAT2' ENTERED AT 11:57:40 ON 16 NOV 2005  
        4 L30

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